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FLUID REPLACEMENT IN SURGICAL STATES

WITH PARTICULAR REFERENCE TO TRANSFUSION OF ASCITIC FLUID: A CLINICAL AND EXPERIMENTAL STUDY

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NEW ORLEANS

The problem of fluid replacement has presented itself both to biologists and to surgeons. In man the loss of water, electrolytes or blood leads to disturbances which are progressive and which alter the normal response to replacement therapy. It is our purpose to present in this paper: (1) a study of the abnormal physiologic picture which results from loss of water, electrolytes and blood; (2) the technic of fluid replacement; (3) a critical evaluation of blood replacement fluids, and (4) the present status of transfusion of ascitic fluid.

The indications for fluid replacement fall into four main groups:

1. Loss of body water.
2. Loss of electrolytes.
3. Loss of whole blood.
4. Loss of plasma.

While it is convenient for purposes of discussion to separate each type of depletion state, in actual practice the distinction is not clearcut, and one will find frequently the merging of one state into another.

LOSS OF BODY WATER

Loss of water from the body in excess of the intake of water results in dehydration. Similarly, desiccation of the blood is known as anhydremia. From the surgical point of view the causes of dehydration may be divided into two groups: (1) exogenous and (2) endogenous. Among the more important exogenous causes are voluntary or enforced deprivation of water, excessive sweating due to sunstroke, heat prostration, traumatic shock and surgical operations. Endogenous causes are prolonged diarrhea due to surgical lesions of the intestinal tract; vomiting

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due to obstructing lesions of the gastrointestinal tract, and inability to swallow liquids due to obstructing lesions of the esophagus.

The physiologic effects of dehydration may be considered at this point. Almost 68 per cent of the total loss of water comes from the muscles (Engels [1]), and the major portion of the remainder from the blood and skin (Durig;[2] Straub;[3] Tobler [4]). The composition of the blood is altered in the presence of dehydration. The specific gravity increases (Rominger [5]), and there is an increased concentration of red blood cells (Czerny [6]) and of hemoglobin (Underhill and Kapsinow [7]). As most of the loss of water from the blood is from the plasma, the concentration of plasma proteins is relatively greater than that of erythrocytes (Keith [8]). Thus plasma protein concentrations 50 to 100 per cent above normal have been reported (Reiss;[9] Marriott;[10] Berend and Tezner [11]). The rate of loss of water is important in determining the degree of hemoconcentration. When water is lost relatively slowly, hemoconcentration is not quite so great (Adolph [12]). When severe dehydration has lasted for some time, destruction of serum proteins, hemoglobin and red blood cells takes place, with a further loss of metabolic water (Lust;[13] Gürber;[14] Utheim [15]). It is evident that an examination of the blood during this stage will give a false impression

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2. Durig, A.: Wassergehalt und Organfunction, Arch. f. d. ges. Physiol. **85**: 401; **87**:42, 1901.

3. Straub, W.: Ueber den Einfluss der Wasserentziehung auf den Stoffwechsel und Kreislauf, Ztschr. f. Biol. **20**:537-566, 1899.

4. Tobler, L.: Ueber Veränderungen im Mineralstoffbestand des Säuglingskörpers bei akuten und chronischen Gewichtsverlusten, Jahrb. f. Kinderh. **73**:566-585, 1911.

5. Rominger, E.: Ueber des Wassergehalt des Blutes des gesunden und des ernährunggestörten Säuglings, Ztschr. f. Kinderh. **26**:23-64, 1920.

6. Czerny, A.: Versuche ueber Bluteindickung und ihre Folgen, Arch. f. exper. Path. u. Pharmakol. **34**:268-280, 1894.

7. Underhill, F. P., and Kapsinow, R.: The Influence of Water Introduction upon Blood Concentration Induced by Water Deprivation, J. Biol. Chem. **54**:459-464, 1922.

8. Keith, N. M.: Blood Volume Changes Following Water Abstinence, Am. J. Physiol. **59**:452-453, 1922.

9. Reiss, E.: Untersuchungen der Blutkonzentration des Säuglings, Jahrb. f. Kinderh. **70**:311-362, 1909.

10. Marriott, W. McK.: Anhydremia, Physiol. Rev. **3**:275-294, 1923.

11. Berend, N., and Tezner, E.: Die Wasserentziehung im Säuglingsorganismus bei akuten Gewichtsschwankungen, Monatschr. f. Kinderh. **10**:212-238, 1911.

12. Adolph, E. F.: The Regulation of the Water Content of the Human Organism, J. Physiol. **55**:114-132, 1921.

13. Lust, F.: Ueber den Wassergehalt des Blutes und sein Verhalten bei den ernährungsstörungen der Säuglinge, Jahrb. f. Kinderh. **73**:85; 179, 1911.

of the degree of dehydration. While the concentration of sodium chloride in the plasma is usually normal (Salge [16]), it may be increased when the dehydration occurs rapidly (Keith [17]). The level of blood phosphate rises as renal function diminishes (Howland and Marriott [18]). An increase in the concentration of nonprotein nitrogen and urea nitrogen occurs as a result of increased destruction of protein and failing renal function (Schloss and Stetson [19]). The level of blood sugar is raised (Marriott [10]), as is that of lactic acid in the blood (Clausen [20]). Definite acidosis is present, as evidenced by the increased hydrogen ion concentration of the venous blood (Sellards and Shakllee [21]).

The blood volume diminishes by as much as 40 to 50 per cent of the initial level, the decrease being mainly in the amount of plasma (Keith;[8] Rogers [22]). As the blood volume diminishes, a compensatory vasoconstriction occurs, leading to a diminished volume flow of blood, particularly in the extremities (Marriott;[10] Utheim [15]). The heart gives evidence of a diminished flow of blood through the coronary arteries, as indicated by the electrocardiogram (McCulloch [23]). The blood pressure, however, is usually not greatly lowered, provided that dehydration and anhydremia are gradual in onset (Feilchenfeld [24]). When anhydremia is produced rapidly in the experimental animal, a state resembling secondary shock with lowered blood pressure supervenes (Davis [25]).

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15. Utheim, K.: A Study of the Blood and Its Circulation in Normal Infants and in Infants Suffering from Chronic Nutritional Disturbances, Am. J. Dis. Child. **20**:366-392 (Nov.) 1920.

16. Salge, B.: Ueber die physikalischen Eigenschaften des Blutes des Säuglings, Ztschr. f. Kinderh. **2**:347-359, 1911.

17. Keith, N. M.: Circulatory Changes in Experimental Dehydration, Am. J. Physiol. **63**:394-395, 1923.

18. Howland, J., and Marriott, W. McK.: Acidosis Occurring with Diarrhea, Am. J. Dis. Child. **11**:309-325 (May) 1916.

19. Schloss, O. M., and Stetson, R. E.: The Occurrence of Acidosis with Severe Diarrhea, Am. J. Dis. Child. **13**:218-230 (March) 1917.

20. Clausen, S. W., cited by Marriott.[10]

21. Sellards, A. W., and Shakllee, A. O.: Indications of Acid Intoxication in Asiatic Cholera, Philippine J. Sc. **6**:53-76, 1911.

22. Rogers, L.: The Treatment of Cholera by Injections of Hypertonic Saline Solutions with a Simple and Rapid Method of Intra-Abdominal Administration, Philippine J. Sc. **4**:99-105, 1909.

23. McCulloch, H.: Studies on the Heart in Nutritional Disturbances in Infancy, Am. J. Dis. Child. **20**:486 (Dec.) 1920.

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The tissue lesions of acute anhydremia are of interest and consist of widespread capillary distention with numerous petechial hemorrhages into the pulmonary alveoli, the subendocardium, the spleen, the leptomeninx and elsewhere. The adrenal glands may show petechial hemorrhages in the cortices and dense infiltration with polymorphonuclear leukocytes (Davis [26]). The question now raises itself: How much loss of water will the body tolerate before death occurs? It is evident that rapidity of loss of water is the most important factor in determining the outcome. In dogs, death will result when an amount of water equivalent to 4 per cent of the body weight is lost rapidly (Davis [27]).

Measurement of Degree of Dehydration.—The methods of determining the degree of dehydration may now be discussed briefly. The clinical manifestations are obvious. The skin becomes wrinkled and dry, and the mucous membranes are lusterless. The eyeballs become soft. As a result of the deficient flow of blood, the extremities are cold. The respirations may be deep and of the "air hunger" type due to acidosis. Various other tests of hydration may be used:

1. Those applicable to the skin:
   (*a*) Standard wheal formation (Ebbecke;[28] Pilcher [29])
   (*b*) Intradermal salt absorption (Aldrich and McClure [30])
   (*c*) Intradermal serum absorption (Ribadeau-Dumas and Tisserand [31])
2. Those applicable to the blood:
   (*a*) Erythrocyte concentration (Schade and Menschel [32])
   (*b*) Hemoglobin concentration (Greene and Rowntree [33])

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27. Davis, H. A.: Relative Significance of Water and of Protein Loss in Dehydration Shock, Proc. Soc. Exper. Biol. & Med. **43**:357-359, 1940.

28. Ebbecke, U.: Capillarerweiterung, Urticaria und Schock, Klin. Wchnschr. **2**:1725-1727, 1923.

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31. Ribadeau-Dumas, L., and Tisserand, D.: Etude sur la résorption des sérums chez les infants atteints d'affections diverses avec dénutrition, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1637-1641, 1925.

32. Schade, H., and Menschel, H.: Ueber die Gesetze der Gewebsquellung und ihre Bedeutung für klinische Frage (Wasseraustausch im Gewebe, Lymphbildung und Oedementstehung), Ztschr. f. klin. Med. **96**:279-327, 1923.

(*c*) Hematocrit reading (Dresel and Leitner [34])

(*d*) Specific gravity of the blood plasma (Moore and Stewart [35])

3. Response to administration of water in terms of:

(*a*) Excretion of urine (Volhard [36])

(*b*) Time curve of blood dilution (Rominger;[5] Davis [37])

(*c*) Rate of oxygen consumption (Davis [38])

In practice one will find that the tests of group 3 provide the most comprehensive picture of the state of the dehydrated patient. The accuracy of the Volhard test will depend on the presence of normal renal function. The fact that in the presence of the severer grades of dehydration a fall in hemoconcentration and in the amount of plasma proteins occurs is a justifiable basis for criticism of the tests of group 2. Moreover, losses of blood occurring during surgical operations will further invalidate such tests. Recently, Hopps and Christopher [39] have reported encouraging results with the McClure-Aldrich test in the estimation of dehydration in surgical patients.

Fluid Replacement in Cases of Dehydration.—It might be pointed out that our discussion at this point will refer only to that form of dehydration which is uncomplicated by gross losses of electrolytes or of blood. Minor grades of dehydration may be treated by water administered by the oral or the rectal route. However, many dehydrated patients require treatment with fluids given intravenously. The response of the dehydrated organism to intravenous fluids must be given consideration (chart 1). The administration of isotonic dextrose solutions leads to a marked increase in the metabolic rate and in oxygen utilization. Coincidentally there occurs an increased breakdown of protein, as evidenced

33. Greene, C. H., and Rowntree, L. G.: Effect of Experimental Administration of Excessive Amounts of Water on Volume and Concentration of Blood, Am. J. Physiol. **80**:209-229, 1927.

34. Dresel, K., and Leitner, Z.: Zur Physiologie und funktionellen Pathologie des Wasserhaushaltes; die Beziehungen der Milz zum Wasserhaushalt, Ztschr. f. klin. Med. **111**:394-419, 1929.

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38. Davis, H. A.: Studies in Water Balance: Excessive Oxygen Usage Response of Dehydrated Animals to Water and Electrolytes, Proc. Soc. Exper. Biol. & Med. **33**:242-244, 1935.

39. Hopps, H. C., and Christopher, F.: The McClure-Aldrich Test in Water Balance Following Operation, Surg., Gynec. & Obst. **69**:637-644, 1939.

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by the augmented output of nitrogenous products in the urine. Intravenous administration of isotonic sodium chloride solution is followed by only a moderate increase in the metabolic rate (Davis [38]). Using these facts as a basis in the replacement therapy of dehydration, we customarily divide dehydrated patients into three groups:

1. Patients showing dehydration with mild anhydremia.
2. Patients showing dehydration with severe anhydremia.
3. Patients with dehydration shock.

The first group comprises those patients who, while exhibiting the usual clinical evidences of dehydration, do not have any lowering of the blood pressure and whose blood reveals an erythrocyte count not exceeding 5,000,000 per cubic millimeter. When fluid replacement by the parenteral route is indicated, one may administer 2,500 cc. of 5 per cent dextrose solution by vein each twenty-four hours until the

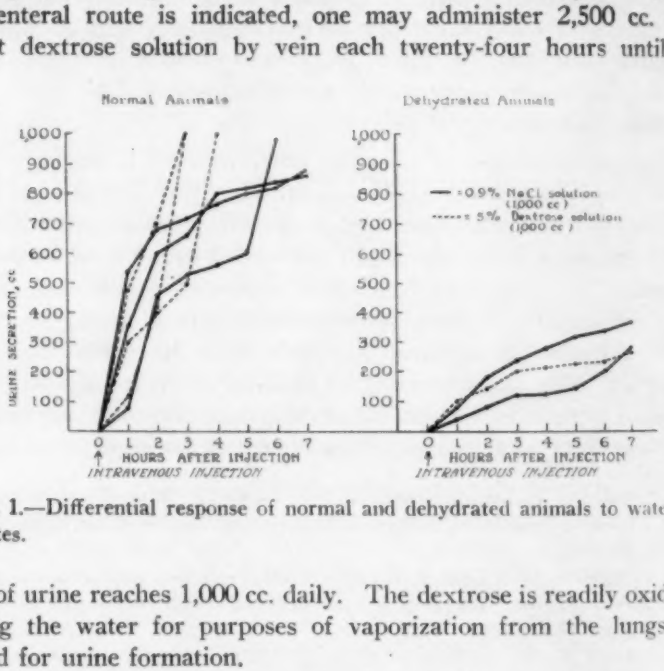

Chart 1.—Differential response of normal and dehydrated animals to water and electrolytes.

output of urine reaches 1,000 cc. daily. The dextrose is readily oxidized, releasing the water for purposes of vaporization from the lungs and skin and for urine formation.

Patients falling into the second group exhibit erythrocyte counts exceeding 5,000,000 per cubic millimeter of blood and some lowering of the systolic blood pressure. Five per cent dextrose solution is used, but only 1,000 cc. is administered in the first twenty-four hours, 1,500 cc. in the second twenty-four hours and 2,000 cc. in the third twenty-four hours. Thereafter, 2,500 cc. is given daily until the volume of urine reaches 1,000 cc. per day. It is essential that the solution be administered slowly, at a rate of 4 to 5 cc. per minute, as the concentrated blood holds the injected fluid for a long period, and, as a result there is present a definite danger of overdistention of the right side of the heart.

In the third group may be placed those persons who manifest the more severe secondary effects of dehydration, namely, anhydremia, reduced blood volume, acidosis, lowering of the oxygen content of the blood, hyperglycemia, diminished volume flow of blood and reduction of the systolic blood pressure. Some of these patients will exhibit symptoms of secondary shock. The blood is concentrated. However, in the later stages there may occur a breakdown of the red blood cells and of the plasma proteins, so that hemoconcentration may be slight or absent. It has been pointed out that pulmonary edema occurs in cases of shock associated with dehydration (Davis [26]). Crystalloid solutions administered by vein at this time will not be retained by the blood but will pass out into the extravascular tissue spaces. Moreover, such solutions will favor an increase of the pulmonary edema. It is apparent that the essential treatment at this point should be directed toward restoring the blood volume. This may be accomplished by preliminary transfusions of whole blood, plasma or ascitic fluid (Davis and White [40]). Thereafter, fluid replacement may proceed along the lines indicated for the patients of group 2. It may be questioned whether electrolyte replacement should be undertaken in the presence of dehydrated states. While there occurs some loss of sodium, potassium and chloride ions (Tobler; [4] Meyer [41]), restitution may be deferred until hydration has been partially accomplished by means of isotonic dextrose solutions.

LOSS OF ELECTROLYTES

The total water content of the body is directly proportional to the number of osmotically active particles present in the tissues. The major portion of these particles is electrolytes. It has been demonstrated by many workers (Gamble and Ross; [42] Gamble and McIver [43]) that sodium is the most important electrolyte in the maintenance of normal osmotic relations between the extracellular and the intracellular fluids. The daily intake of salt varies from 3 to 10 Gm.; of which 1 to 2 Gm. is derived from food. Approximately 0.2 Gm. of sodium chloride is lost per day in the stools (Welch, Masson and Wakefield [44]) and 0.25 to 0.41 Gm.

40. Davis, H. A., and White, C. S.: Human Ascitic Fluid as a Blood Substitute in Experimental Secondary Shock, Proc. Soc. Exper. Biol. & Med. **38**: 462-465, 1938.

41. Meyer, L. F.: Ueber den Wasserbedarf des Säuglings, Ztschr. f. Kinderh. **5**:1-30, 1912.

42. Gamble, J. L., and Ross, S. G.: Factors in Dehydration Following Pyloric Obstruction, J. Clin. Investigation **1**:403-423, 1925.

43. Gamble, J. L., and McIver, M. A.: Acid-Base Composition of Gastric Secretion, J. Exper. Med. **48**:837-847, 1928.

44. Welch, C. S.; Masson, J. C., and Wakefield, E. G.: Clinical and Laboratory Findings After Excessive Loss of Intestinal Fluid from the Ileum, Surg., Gynec. & Obst. **64**:617-621, 1937.

by insensible perspiration (Freyberg and Grant [45]), while the remaining excess is excreted by the kidneys. The various gastrointestinal secretions contain electrolytes, the basic sodium ion being found in the pancreatic juice and bile and the acidic chloride ion in the gastric juice. Under normal circumstances the electrolytes in these juices are reabsorbed, and thus no loss from the body occurs. However, if failure of reabsorption occurs, as it does in certain surgical conditions, a therapeutic problem arises. In clinical states, loss of water usually accompanies loss of electrolytes. It is not this loss of water which is significant but rather the fact that as the total amount of electrolytes diminishes the ability of the organism to retain water decreases proportionately.

Physiologic Effects of Loss of Electrolytes.—It is necessary to distinguish the effects of loss of electrolytes per se from those of secondary dehydration. In animals in which a loss of electrolytes is produced by means of a gastric fistula (Dragstedt and Ellis [46]) or by means of a pancreatic fistula (Dragstedt, Montgomery and Ellis [47]), there occur gradually increasing muscular weakness, loss of appetite and a tendency to muscular tremors. Terminal convulsions may occur. If sodium mainly is lost, acidosis occurs, and if chloride is lost, alkalosis develops. Other phenomena, such as hemoconcentration, decrease in the output of urine and diminution in the amount of gastric and pancreatic juice secreted, may be attributed to secondary dehydration. In man the rapid loss of electrolytes results in muscular cramps and fatigue. The effects of the gradual loss of electrolytes in man have been investigated by McCance [48] and others. Anorexia, nausea and a tendency toward muscular fatigue and cramps were prominent symptoms. Mental fatigue, inability to concentrate and slowness of mental reactions were noted. There was a fall in the level of plasma and corpuscular chlorides and in that of serum sodium, with an increase in the level of serum potassium. The blood pressure was unchanged in spite of a presumptive reduction of the blood volume as evidenced by hemoconcentration. While these changes comprised the effects of loss of salt, others, equally definite, could be attributed to the resultant dehydration. Among the latter were severe loss of weight, hemoconcentration with respect to erythrocytes and hemoglobin, increase in plasma proteins and blood urea and a nega-

45. Freyberg, R. H., and Grant, R. L.: Loss of Minerals Through the Skin of Normal Humans When Sweating Is Avoided, J. Clin. Investigation **16**:729-731, 1937.

46. Dragstedt, L. R., and Ellis, J. C.: Fatal Effect of Total Loss of Gastric Juice, Am. J. Physiol. **93**:407-410, 1930.

47. Dragstedt, L. R.; Montgomery, M. L., and Ellis, J. C.: New Type of Pancreatic Fistula, Proc. Soc. Exper. Biol. & Med. **28**:109-110, 1930.

48. McCance, R. A.: Medical Problems in Mineral Metabolism: Experimental Human Salt Deficiency, Lancet **1**:823-830, 1936.

tive nitrogen balance. It is apparent, therefore, that the sequence of events initiated by loss of electrolytes, particularly sodium, ends in dehydration with anhydremia, progressive reduction of the blood volume and, finally, generalized anoxemia, shock and death.

Surgical Causes of Loss of Electrolytes.—While as much as 2 Gm. of salt may be lost each hour in the perspiration when sweating is excessive (Dill, Jones, Edwards and Oberg [49]), this is not a common source of depletion in surgical patients. More common, however, is a loss of electrolytes via the gastrointestinal secretions. Vomiting due to obstruction of various portions of the alimentary canal results in loss of gastric juice, succus entericus, pancreatic juice or bile. The predominant electrolyte in gastric juice is the chloride ion, and loss of this results in hypochloremia and alkalosis. In bile, pancreatic juice and succus entericus the principal electrolyte is sodium, and loss of this ion is followed by acidosis. The production of artificial openings in the intestinal tract, e. g., by jejunostomy, ileostomy or cecostomy, may result in a considerable loss of unabsorbed electrolytes. Prolonged drainage from a biliary fistula may lead to extensive depletion of the sodium ion and to acidosis. Similarly, prolonged diarrhea, in which the electrolytes are removed from the body before reabsorption occurs, leads to loss of the sodium ion and to acidosis. The loss of electrolytes in the discharges from suppurating wounds may be significant. In addition, prolonged use of Wangensteen or Miller-Abbott gastrointestinal tubes may result in severe depletion of water and electrolytes.

Measurement of Degree of Electrolyte Loss.—The degree of loss of electrolytes may be determined either directly or indirectly. Estimation of the level of plasma sodium chloride, which varies normally from 560 to 630 mg. per hundred cubic centimeters of blood, gives a direct clue to the extent of electrolyte loss. A study of the secondary effects of electrolyte loss provides an indirect method of evaluating its extent. This may be done in two ways:

1. Estimation of the carbon dioxide–combining power of the plasma.
2. Estimation of the degree of secondary dehydration by means of blood studies, erythrocyte count, hemoglobin determination, etc.

When the basic ions, such as sodium, are lost, acidosis results, and the carbon dioxide–combining power of the plasma falls to or below 50 volumes per cent.

Conversely, if a depletion of the acidic ions, such as the chlorides, occurs, alkalosis develops, and the carbon dioxide–combining power of

49. Dill, D. B.; Jones, B. F.; Edwards, H. T., and Oberg, S. A.: Salt Economy in Extreme Dry Heat, J. Biol. Chem. **100**:755-767, 1933.

the plasma is elevated to or above 70 volumes per cent. The methods of determining the grade of secondary dehydration have been discussed previously and will be only mentioned at this point.

Fluid Replacement.—The therapeutic problem with patients suffering from loss of electrolytes centers around the resultant dehydration, as the loss of electrolytes per se is self limited. It is the inability of the salt-depleted organism to retain water, while the output of water continues via the skin, lungs and urine, which leads, finally, to a fatal reduction of the blood volume. Before considering the various replacement fluids, it might be pertinent to discuss briefly the response to fluids of the organism suffering from electrolyte depletion and dehydration (chart 2). Dogs which have been depleted of chlorides and in which alkalosis has developed show an increased ability to retain 5 per cent dextrose solu-

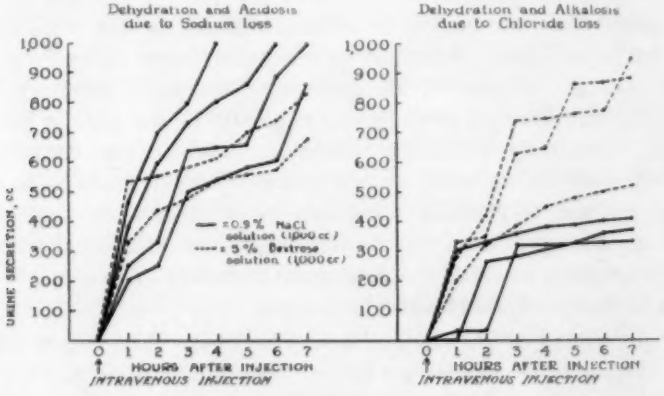

Chart 2.—Differential response of dehydrated animals with acidosis and with alkalosis to water and electrolytes.

tion and 0.9 per cent sodium chloride solution injected intravenously. However, retention of sodium chloride solution is relatively much greater than that of dextrose solution and corresponds with that observed in animals which have been dehydrated by deprivation of water. On the other hand, animals which have suffered a loss of sodium base resulting in dehydration with acidosis reveal an incapacity to retain either isotonic dextrose or sodium chloride solution given by vein. The rate of escape of water from such an animal is subject to some interesting variations. When an extensive loss of basic ions has occurred and fluid replacement takes the form of administration of 5 per cent dextrose solutions, the administration of isotonic solution of sodium chloride may precipitate a diuresis (Davis and Dragstedt [50]). The explanation of this paradoxic

50. Davis, H. A., and Dragstedt, L. R.: The Relative Significance of Electrolyte Concentration and Tissue Reaction in Water Metabolism, Am. J. Physiol. **113**:193-199, 1935.

phenomenon may be that the loss of base is such that the body fluids become relatively hypotonic. Physiologic solution of sodium chloride is then hypertonic with respect to the body fluids and when administered provokes a flow of interstitial fluid into the blood vessels and an increased output of urine.

Somewhat analogous results were obtained by McCance and his associates in human beings suffering from loss of sodium. In such persons

TABLE 1.—*Types of Blood Substitutes*

A. Whole or Partial Blood
  (a) Fresh
    1. Whole blood } Donors
    2. Citrated blood } Autotransfusion
    3. Blood plasma or serum
    4. Defibrinated blood
  (b) Preserved
    1. Living donor's blood
    2. Placental blood
    3. Cadaver blood
    4. Blood plasma and serum
    5. Human ascitic fluid
    6. "Lyophile" plasma and serum
    7. "Lyophile" ascitic fluid
    8. Hemoglobin in Ringer's solution

B. Artificial Substitutes for Blood
  1. Acacia in saline solution
  2. Gelatin-saline solution
  3. Amino acid solution
  4. Isotonic dextrose solution
  5. Modifications of electrolyte solutions:
    (a) Isotonic sodium chloride solution (0.85%)
    (b) Ringer's solution *
    (c) Ringer-Locke's solution †
    (d) Tyrode solution ‡
    (e) Normet's solution §
    (f) Hartmann-Senn solution ¶
    (g) Dextrose-saline solution

* Ringer's solution: 0.95% sodium chloride, 0.02% potassium chloride, 0.02% calcium chloride.

† Ringer-Locke solution: 0.9% sodium chloride, 0.042% potassium chloride, 0.024% calcium chloride, 0.1% dextrose, 0.2% sodium bicarbonate, saturated with oxygen.

‡ Tyrode solution: 0.8% sodium chloride, 0.02% potassium chloride, 0.02% calcium chloride, 0.01% magnesium chloride, 0.005% sodium dihydrogen phosphate, 0.1% sodium bicarbonate, 0.1% dextrose.

§ Normet's solution: 22 Gm. of sodium citrate, 6.5 Gm. of neutral calcium citrate, 4.5 Gm. of neutral magnesium citrate, 1 Gm. of iron ammonium citrate, 0.15 Gm. of manganese citrate, 1,000 cc. distilled water; 20 cc. of this mixture to 1,000 cc. 0.7% sodium chloride solution.

¶ Hartmann-Senn solution: 100 cc. 85% lactic acid solution, 700 cc. distilled water; sufficient concentrated sodium hydroxide to make the solution alkaline; distilled water to 1,000 cc.

the diuresis following the ingestion of water was greatly delayed. In addition, the ingestion of salt caused at first a loss of body water and a decrease in weight. It is evident that such abnormal responses to administration of salt and water to sodium-depleted persons must be considered in treatment by replacement of water and electrolytes.

The use of hypertonic solutions of electrolytes is contraindicated, for the reasons already given. Various types of isotonic electrolyte solutions are available (table 1). Coller and Maddock [51] have expressed

51. Coller, F. A., and Maddock, W. G.: The Water Requirements of Surgical Patients, Ann. Surg. **98**:952-960, 1933.

preference for Ringer's solution. Hartmann and others [52] recommended a solution containing sodium lactate. The lactate is oxidized, leaving the base free. We have found that an isotonic solution of 5 per cent dextrose with 0.9 per cent sodium chloride provides an excellent replacement fluid. The estimated abnormal electrolyte loss plus the basic electrolyte requirement provides a clue to the amount of solution to be administered. The general principles of fluid replacement for this group of patients are similar to those obtaining in cases of dehydration without electrolyte loss. Again, emphasis must be placed on the secondary dehydration. If this has reached the stage of reduction of blood volume, the primary treatment is directed toward its restoration to a normal level by means of blood transfusion or, better still, by plasma or ascitic fluid transfusion. Thereafter, electrolyte solutions may be administered. If the possibility of secondary reduction of the plasma volume and of the plasma proteins as a result of dehydration is not given consideration, injection of electrolyte solutions even in moderate amounts may be followed by edema. This is well illustrated by case 1.

CASE 1.—A white man aged 74 years was admitted to the Charity Hospital of Louisiana at New Orleans suffering from a carcinoma of the esophagus. Extreme dehydration and anhydremia were present, associated with hemoconcentration and increased concentration of the plasma proteins. Fluid replacement by vein was begun, 2,500 cc. of 5 per cent dextrose in 0.9 per cent sodium chloride solution being used daily. On the third day edema of the lower extremities developed, and bubbling rales could be auscultated at the bases of both lungs. It is evident that in this patient there was a diminution in the plasma volume and in the total amount of plasma proteins, in spite of their apparent concentration.

The type of electrolyte lost has an important bearing on the therapeutic problem in this group of cases. When sodium is lost, with resultant acidosis and dehydration, relatively larger amounts of solutions of electrolytes may be administered, as neither the electrolytes nor the water will be well retained, and there is less danger of retention edema. The adjunct use of desoxycorticosterone acetate will help to fix the sodium and, consequently, the water in the tissues. With loss confined mainly to the chloride ion and resulting in alkalosis and dehydration, relatively smaller amounts of electrolyte solutions may be given, as both water retention and electrolyte retention are greater (Davis and Dragstedt [50]).

LOSS OF WHOLE BLOOD

Whole blood may be lost externally, into body cavities and into tissues. The causes of such loss are too well known to require enumeration here. The physiologic effects are dependent on the ensuing reduction of the blood volume. The removal of 500 cc. of blood has little

52. Hartmann, A. F.; Senn, M. J. E.; Nelson, M. V., and Perley, A. M.: Use of Acacia in Treatment of Edema, J. A. M. A. **100**:251-254 (Jan. 28) 1933.

effect on the blood pressure, and the blood volume is restored within one hour. The loss of 1,000 cc. of blood or more is usually followed by a fall of blood pressure. Recovery is possible after losses up to 30 per cent of the blood volume. Beyond 30 per cent the ability of the organism to restore the lost volume of blood is insufficient, and death results. The immediate effects of hemorrhage are an increase in the heart rate and the respiratory rate, contraction of the spleen and generalized vasoconstriction. A regional redistribution of blood follows hemorrhage (Davis and Jermstad [53]). Owing to marked constriction of the blood vessels in the splanchnic area, an outflow of blood from that area takes place toward the thoracic region. As a result of the reduced blood volume, a diminution of the volume flow of blood and of the metabolic rate develops. The various elements of the lost blood are replaced at differing rates. Water passes rapidly from the interstitial tissue spaces into the blood stream in order to increase the blood volume. This water contains relatively little protein, so that protein regeneration, which is dependent on the liver, takes several days to be completed. The cellular element is the last to be restored, the erythrocytes not regaining their normal numbers until several weeks have passed.

Measurement of the Degree of Blood Loss.—The extent of loss of blood may be gaged approximately by noting the clinical manifestations and by making determinations of the values for erythrocytes, hemoglobin and blood pressure. These are too well known to require elaboration here.

Fluid Replacement.—Various fluids have been advocated for replacement of blood. It is obvious that fresh whole blood is the most efficacious fluid. However, this is expensive, is not always available and is incapable of storage beyond three weeks. As a result, a search for an efficient substitute for whole blood has developed. An ideal substitute for blood should possess the following properties:

1. It should be readily available.
2. It should be effective.
3. It should be capable of prolonged storage without deteriorating.
4. It should be nontoxic even when administered in large quantities.
5. It should contain one or more of the elements of blood.
6. It should possess one or more of the biologic properties of blood; for example, ability to transport oxygen or ability to maintain the colloidal osmotic pressure.

53. Davis, H. A., and Jermstad, R. J.: Regional Redistribution of Blood in Experimental Secondary Shock, Arch. Surg. **38**:556-580 (March) 1939.

One may apply these criteria to the fluids which have been advocated for use as blood substitutes (table 1).

Crystalloid Solutions: It is apparent that crystalloid solutions cannot be regarded as adequate substitutes for blood, since they do not contain either proteins or hemoglobin. However, in circumstances in which the loss of blood has not been excessive they may exert a favorable influence. When the reduction in blood volume has existed long enough to produce, through oxygen lack, increased permeability of the capillary walls, administration of such solutions may result in a further loss of plasma proteins from the blood stream (Beard and Blalock;[54] Davis[55]) and a reduction in the utilization of oxygen by the organism (Davis[55]). Much disagreement exists regarding the value of crystalloid solutions in the treatment of hemorrhage. MacFee and Baldridge[56] and Hoitink[57] have stated that such solutions are useful, while others have expressed the opposite opinion. This difference of opinion would disappear if it were recognized that it is the factor of capillary permeability which determines the degree of efficacy of such solutions (chart 3). The crystalloid-containing fluids which have been recommended for use are given in table 1. It is possible that certain of the beneficial effects of such fluids can be attributed to their action on the cardiovascular system. Normet's[58] fluid (table 1) contains various citrates which not only stimulate the heart but cause vasoconstriction. In Hartmann-Senn solution (table 1) there is present sodium R-lactate, which acts as a buffer and helps to overcome either alkalosis or acidosis. In animals, administration of crystalloid solutions in excessive amounts results in pulmonary edema (Davis[55]). This fact should be remembered when such fluids are administered to patients suffering from loss of whole blood with resultant alteration of capillary permeability.

Acacia Solution: While solutions of acacia were injected into animals as early as 1881, their first deliberate use as fluids for replacement

54. Beard, J. W., and Blalock, A.: Intravenous Injections: A Study of the Composition of the Blood During Continuous Trauma to the Intestines When No Fluid Is Injected and When Fluid Is Injected Continuously, J. Clin. Investigation **11**:249-265, 1932.

55. Davis, H. A.: Physiological Availability of Fluids in Secondary Shock. Arch. Surg. **35**:461-477 (Sept.) 1937.

56. MacFee, W. F., and Baldridge, R. R.: Post-Operative Shock and Shock-Like Conditions: Treatment by Infusion in Large Volumes, Ann. Surg. **91**:329-341, 1930.

57. Hoitink, A. W. J. H.: Treatment of Acute Fatal Hemorrhage by Injection of Artificial Blood Substitutes, Surg., Gynec. & Obst. **61**:613-622, 1935.

58. Normet, L.: Traitement des hémorrhagies expérimentales chez le chien par un sérum artificial à base de citrates, Compt. rend. Acad. d. sc. **188**:354-356. 1929.

of blood after hemorrhage did not take place until 1906 (Morawitz [59]). Since that time various investigators have shown that acacia solutions (6 per cent in 0.9 per cent sodium chloride or 5 per cent dextrose solutions) are capable of raising the blood pressure and maintaining the blood volume after hemorrhage (Bayliss [60]). Unsatisfactory results have been reported, however, with acacia solutions after loss of blood (Kruse; [61] Henderson and Haggard; [62] Tsurumaki and Kurozawa [63]). The permeability of the capillaries increases when the low blood pressure following loss of blood is allowed to persist. The presence of this factor may influence the results obtained and may explain the observations of Penfield,[64] who noted that acacia solutions were not more effective in saving shocked animals than was isotonic solution of sodium

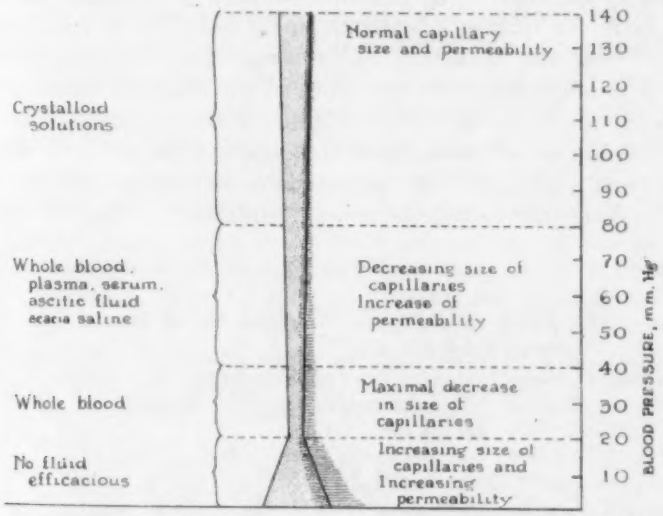

Chart 3.—**Shock due to loss of whole blood; efficacy of replacement fluids in relation to capillary permeability.**

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59. Morawitz, P.: Ueber einige postmortale Blutveränderungen, Beitr. z. Physiol. **8**:1-14, 1906.

60. Bayliss, W. M.: The Use of Gum Solutions for Intravenous Injection, Brit. M. J. **1**:564, 1917.

61. Kruse, T. K.: The Pharmacology of Acacia, Am. J. Physiol. **49**:137, 1919.

62. Henderson, Y., and Haggard, W. H.: Hemorrhage as a Form of Asphyxia, J. A. M. A. **78**:697-704 (March 11) 1922.

63. Tsurumaki, T., and Kurozawa, R.: Intravenous Infusion of Physiological Salt and Ringer-Locke's Solution Containing Gum Arabic, Acta scholae med. univ. imp. in Kioto **6**:471-497, 1924.

64. Penfield, W. G.: Treatment of Severe and Progressive Hemorrhage by Intravenous Injections, Am. J. Physiol. **48**:121, 1919.

chloride. Hurwitz [65] was the first to administer acacia solutions to human beings. His work was followed by that of Bayliss,[60] Coburn and Ward [66] and Good, Mugrage and Weiskittel,[67] all of whom reported the successful use of such solutions.

Acacia solutions, nevertheless, are not devoid of toxicity. Deaths have followed their use (Lee [68]). Anaphylactic reactions to acacia occur in man and in guinea pigs (Maytum and Magath [69]). Acacia solutions in vitro produce agglutination of the red blood cells (Lucia and Brown [70]). They may also lower the oxygen content of the blood by coating the red blood cells (Christie, Phatak and Olney [71]). The last-mentioned fact may render their use dangerous when the red cell count has been reduced to very low levels by hemorrhage. Acacia is engulfed by the cells of the reticuloendothelial system and may remain in the body for months (Andersch and Gibson [72]) or even for years (Keith, Power and Wakefield [73]). Regeneration of plasma proteins by the liver is interfered with, and repeated injections of acacia solutions may lead to hypoproteinemia (Dick, Warweg and Andersch [74]). Finally, it has been demonstrated that acacia solutions leave the blood stream fairly readily and cannot maintain the osmotic pressure of the blood for more than forty-eight hours (Huffman [75]). Each of the fluids

65. Hurwitz, S. H.: Acacia Solutions, J. A. M. A. **68**:699 (March 3) 1917.

66. Coburn, R. C., and Ward, G. G.: Blood Pressure in Operative Surgery and General Anesthesia with Especial Reference to the Use of Gum Glucose, S. Clin. North America **5**:548-553, 1925.

67. Good, R. W.; Mugrage, R., and Weiskittel, R.: Acacia Solution in Treatment of Surgical Shock: Analysis of One Hundred and Eleven Case Histories, Am. J. Surg. **25**:134-139, 1934.

68. Lee, R. Van A.: Sudden Death in Two Patients Following Intravenous Injection of Acacia, J. A. M. A. **79**:726-728 (Aug. 26) 1922.

69. Maytum, C. K., and Magath, T. B.: Sensitivity to Acacia, J. A. M. A. **99**:2251-2252 (Dec. 31) 1932.

70. Lucia, S. P., and Brown, J. W.: Suspension Stability of Erythrocytes in Solution of Gum Acacia, Proc. Soc. Exper. Biol. & Med. **32**:189-192, 1934.

71. Christie, A.; Phatak, N. M., and Olney, M. B.: Effect of Intravenous Acacia on Physico-Chemical Properties of Blood, Proc. Soc. Exper. Biol. & Med. **32**:670-672, 1935.

72. Andersch, M., and Gibson, R. B.: Studies on Effects of Intravenous Injections of Colloids: Deposition of Acacia in Liver and Other Organs and Its Excretion in Urine and Bile, J. Pharmacol. & Exper. Therap. **52**:390-407, 1934.

73. Keith, N. M.; Power, M. H., and Wakefield, E. G.: Detection and Persistence of Acacia in Blood, Proc. Staff Meet., Mayo Clin. **10**:38-41, 1935.

74. Dick, M. W.; Warweg, E., and Andersch, M.: Acacia in Treatment of Nephrosis, J. A. M. A. **105**:654-657 (Aug. 31) 1935.

75. Huffman, L. D.: Solution of Acacia and Sodium Chloride in Hemorrhage and Shock: Effect of Intravenous Administration, J. A. M. A. **93**:1698-1702 (Nov. 30) 1929.

discussed has a serious disadvantage, as none possesses any of the normal constituents of blood. The therapeutic problem becomes somewhat clarified when one deals with replacement fluids which contain one or more of these constituents. Those fluids will now be considered.

Preserved Blood: The transfusion of preserved blood was first performed by Hédon [76] in 1902. During the World War (1914 to 1918) preserved blood was used in human beings by Robertson.[77] Little was done with this substitute for fresh blood until it was reintroduced by Jeanneny and his co-workers [78] and by Palazzo and Tenconi [79] in 1934. Despite the use of various blood-preservative solutions, such as sodium citrate solution, Rous-Turner solution and I. H. T. solution,[79a] the safe maximal period of preservation of whole blood does not exceed three weeks. The incidence of post-transfusion reactions increases with the period of preservation. In most respects, however, preserved blood retains the biologic properties of fresh blood. There are many difficulties associated with the maintenance of an adequate supply of preserved blood from living donors. For that reason, the use of placental blood has been advocated (Barenboym and Kaplan;[80] Bruskin and Farberova;[81] Goodall and others [82]). However, only 50 to 70 cc. of blood can be obtained from the average placenta, and a high incidence of staphylococcic contamination has been reported (Hawkins and Brewer [83]). Applying to man the experimental work of Shamov [84]

76. Hédon, M.: Transfusion après les hémorrhagies de globules rouges en suspension dans du sérum artificiel, Arch. de méd. expér. **14**:297, 1902.

77. Robertson, O. H.: Transfusion with Preserved Red Blood Cells, Brit. M. J. **1**:691-695, 1918.

78. Jeanneny, G.; Servantié, L., and Viéroz, J.: Transfusion du sang conservé plusieurs jours en pratique médico-chirurgicale courante, J. de méd. de Bordeaux **111**:685-686, 1934.

79. Palazzo, R., and Tenconi, J.: Transfusión de sangre conservada, Semana méd. **2**:1179-1193, 1934.

79a. Rous-Turner solution: 3.8 per cent sodium citrate and 5.6 per cent dextrose. I. H. T. solution: 5 Gm. of sodium citrate, 7 Gm. of sodium chloride, 0.2 Gm. of potassium chloride, 0.006 Gm. of magnesium sulfate and 1,000 cc. of distilled water.

80. Barenboym, S. I., and Kaplan, A. V.: Transfusion of Placental Blood: Preliminary Report, Sovet. khir. **7**:205-212, 1934.

81. Bruskin, M., and Farberova, P. S.: Use of Umbilical and Placental Blood for Massive Transfusions in Surgical Clinic, Sovet. vrach. zhur. **20**:1546-1551, 1936.

82. Goodall, J. R.; Anderson, F. O.; Altimas, G. T., and MacPhail, F. L.: Inexhaustible Source of Blood for Transfusion and Its Preservation: Preliminary Report (on Placental Blood), Surg., Gynec. & Obst. **66**:176-178, 1938.

83. Hawkins, J., and Brewer, H. F.: Placental Blood, Lancet **1**:132-134, 1939.

84. Shamov, W. N.: Transfusion of Stored Cadaver Blood, Lancet **2**:306-309, 1937.

on animals, Judine [85] has utilized the blood obtained from cadavers for transfusion. As much as 1,500 cc. of blood may be obtained from a single cadaver. The incidence of post-transfusion reactions is high—21 per cent—and several fatalities have occurred (Judine and Skundina [86]). In spite of the fact that fresh defibrinated blood is known to be very toxic (Moldovan [87]), Behr [88] has used it for transfusion, reporting a 17 per cent incidence of reactions.

Hemoglobin in Solution: The functional value of hemoglobin in solution has been investigated with a view to its possible use for blood replacement. Hemoglobin dissolves readily in isotonic salt solutions and in this form takes up oxygen more rapidly than does intracellular hemoglobin (Hartridge and Roughton [89]). It exerts in solution a definite colloidal osmotic pressure which is greater than that of the plasma proteins (Adair;[90] Wells, Miller and Drake [91]). These facts have induced Amberson and his co-workers [92] to utilize 12 to 14 per cent hemoglobin in Ringer's solution as a replacement fluid for blood. They found that almost complete replacement of blood might be accomplished, the animals exhibiting a normal behavior as long as the hemoglobin concentration was maintained at a high level. When the concentration of hemoglobin fell below 3 per cent, death from asphyxia occurred. This form of extracellular hemoglobin leaves the blood stream quickly and, since it is soon converted into methemoglobin, becomes incapable of carrying oxygen. During the process of excretion the kidneys become the site of deposition of methemoglobin. The use of

85. Judine, S.: La transfusion du sang de cadavre à l'homme, Paris, Masson & Cie, 1933, p. 144.

86. Judine, S., and Skundina, G.: Das Problem der Leichenbluttransfusion, Wien. med. Wchnschr. **84**:817-822, 1934.

87. Moldovan, J.: Ueber die Wirkung intravaskulärer Injektionen frischen, defibrinierten Blutes und ihre Beziehungen zur Frage der Transfusion, Deutsche med. Wchnschr. **36**:2422-2425, 1910.

88. Behr, W.: Unsere Erfahrungen mit der Übertragung defibrinierten Blutes, Med. Klin. **29**:156-157, 1933.

89. Hartridge, H., and Roughton, F. J. W.: Rate of Distribution of Dissolved Gases Between Red Blood Corpuscles and Its Fluid Environment: Preliminary Experiments on Rate of Uptake of Oxygen and Carbon Monoxide by Sheep's Corpuscles, J. Physiol. **62**:232-242, 1927.

90. Adair, G. S.: Hemoglobin System: Reproduction of Carbon Dioxide Curves of Blood with an Artificial Mixture of Hemoglobin and Sodium Bicarbonate, J. Biol. Chem. **63**:515-516, 1925.

91. Wells, H. S.; Miller, D. G., Jr., and Drake, B. M.: Validity of Rapid Determinations of Osmotic Pressure of Protein Solutions, J. Clin. Investigation **14**:1-6, 1935.

92. Amberson, W. R.; Mulder, A. G.; Steggerda, F. R.; Flexner, J., and Pankratz, D. S.: Mammalian Life Without Red Corpuscles, Science **78**:106-107, 1933.

5 per cent hemoglobin in Ringer's solution for human beings has been attended by severe reactions (O'Shaughnessy and others [93]). It is evident that hemoglobin in solution does not represent, at its present stage of development, a practical blood replacement fluid.

Blood Plasma and Blood Serum: Although both blood plasma and blood serum contain vasopressor (Bayliss and Ogden [94]) and vasodepressor (Stewart and Harvey; [95] Freund [96]) substances, this fact has not prevented their use as blood replacement fluids. Despite the lack of hemoglobin, the physiologic availability of plasma and serum as substitutes for blood after hemorrhage has been demonstrated in animals (Guthrie and Pike; [97] Rossius; [98] Kallius [99]). Plasma apparently is more efficacious than serum (Richet, Brodin and Saint-Girons [100]). Plasma transfusions in human beings have been used for purposes of hemostasis (Burceva [101]), for hemorrhagic shock (Filatov and Kartaševskij [102]), for traumatic shock (Filatov and Kartaševskij [102]) and for hemolytic shock (Heinatz and Sokolow [103]). The incidence of post-transfusion reactions has been high, varying from 34 per cent (Burceva [101]) to 67.6 per cent (Alovski and Burceva [104]). The plasma from

93. O'Shaughnessy, L.; Mansell, H. E., and Slome, D.: Haemoglobin Solution as a Blood Substitute, Lancet **2**:1068-1069, 1939.

94. Bayliss, L. E., and Ogden, E.: "Vasotonins" and the Pump-Oxygenator-Kidney Preparation, J. Physiol. **77**:34-35, 1933.

95. Stewart, H. A., and Harvey, S. C.: The Vasodilator and Vasoconstrictor Properties of Blood Serum and Plasma, J. Exper. Med. **16**:103-125, 1912.

96. Freund, H.: Ueber die pharmakologischen Wirkungen des defibrinierten Blutes, Arch. f. exper. Path. u. Pharmakol. **86**:266-280, 1920.

97. Guthrie, C. C., and Pike, F. H.: The Relation of the Activity of the Excised Mammalian Heart to Pressure in the Coronary Vessels and to Its Nutrition, Am. J. Physiol. **18**:14-38, 1907.

98. Rossius, L.: Ein tierexperimentellen Beitrag zur Frage der Bluttransfusion, Arch. f. klin. Chir. **137**:583-618, 1925.

99. Kallius, H. U.: Die Verweildauer der gebräuchlichen Blutersatzflüssigkeiten, insbesondere transfundierten Serums nach grossen Blutverlusten im Tierexperiment, Deutsche Ztschr. f. Chir. **220**:216-238, 1929.

100. Richet, C.; Brodin, P., and Saint-Girons, F.: Des injections de plasma sanguin (plasmothérapie) pour remplacer le sang total, Compt. rend. Acad. d. sc. **167**:618, 1918.

101. Burceva, E.: Transfusion kleiner konservierter Plasmamengen zwecks Blutstillung, Arch. f. klin. Chir. **182**:710-717, 1935.

102. Filatov, A., and Kartaševskij, N.: Die Transfusion von menschlichem Blutplasma als blutstillendes Mittel, Zentralbl. f. Chir. **62**:441-445, 1935.

103. Heinatz, S. W., and Sokolow, N. I.: Plasmatransfusion als Methode der Wahl in der Behandlung des hämolytischen Schocks, Zentralbl. f. Chir. **62**:1753-1755, 1935.

104. Alovski, A., and Burceva, E.: Die Transfusion von konserviertem Blutplasma bei gynäkologischen Blutungen, Monatschr. f. Geburtsh. u. Gynäk. **105**:38-46, 1937.

group AB blood does not agglutinate the red blood cells of other blood groups and may be used without preliminary cross-matching tests. Lyophile plasma and serum prepared by the method of Flosdorf and Mudd [105] have been used successfully for replacement of whole blood after hemorrhage in animals (Bond and Wright;[106] Mahoney [107]). These workers have noted a high incidence of reactions following the introduction of lyophile preparations into man. Earlier investigators had noted the occurrence of shock after the use of concentrated serums (Achard, Levy and Gallais [108]). It is apparent from these observations that blood plasma and serum constitute an acceptable form of blood substitute in conditions resulting from loss of whole blood, provided that sufficient hemoglobin remains in the blood stream to carry on oxygen transportation.

Human Ascitic Fluid: Human ascitic fluid as a blood substitute has been investigated both with animals (Davis and White [40]) and with man (Davis and Blalock [109]). The fluid is obtained from patients suffering from ascites due to cardiac failure or to portal cirrhosis of the liver, from whom it is frequently necessary to remove 12 to 15 liters of fluid every two to three weeks. The fluid is sterile and, if removed with aseptic precautions, can be stored in sterile flasks at temperatures of 0 to 5 C. for periods up to five months or longer. In our earlier work with this fluid no preservatives or anticoagulants were used. However, of late we have been adding sodium citrate (50 cc. of a sterile 5 per cent solution) to each 1,000 cc. of ascitic fluid. This prevents the formation of fibrin clots in the fluid and may obviate the possible occurrence of so-called "serum reactions." Recently we have established an "ascitic fluid bank" in the surgical research laboratory of this department, from which fluid can be withdrawn for use in the Charity Hospital. The fluid is submitted to several examinations, namely, the Kahn test, blood agar culture and quantitative determination of the protein and electrolyte content. In a series of specimens of ascitic

105. Flosdorf, E. W., and Mudd, S.: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunol. **29**:389-425, 1935.

106. Bond, D. D., and Wright, D. G.: Treatment of Hemorrhage and Traumatic Shock by the Intravenous Use of Lyophile Serum, Ann. Surg. **107**:500-510, 1938.

107. Mahoney, E. B.: A Study of Experimental and Clinical Shock with Special Reference to Its Treatment by the Intravenous Injection of Preserved Plasma, Ann. Surg. **108**:178-193, 1938.

108. Achard, C.; Levy, J., and Gallais, F.: Recherches expérimentales sur quelques modifications colloïdales produites dans le sérum sanguin par l'injection de sérum concentré et par les saignés plasmatiques, Compt. rend. Acad. d. sc. **194**:1773-1777, 1932.

109. Davis, H. A., and Blalock, J. F.: Autologous and Homologous Transfusion of Human Ascitic Fluid, J. Clin. Investigation **18**:219-224, 1939.

fluid the total protein content was found to vary from 2 to 3.19 Gm. per hundred cubic centimeters; the albumin-globulin ratio from 1.1 : 1 to 2.3 : 1, and the sodium chloride content from 700 to 750 mg. per hundred cubic centimeters. As group-specific agglutinins are present in peritoneal transudates (Weil and Isch-Wall;[110] Yosida;[111] Schiff[112]), it is necessary to cross match the ascitic fluid with the blood of the prospective recipient. This is performed by mixing two drops of ascitic fluid with one drop of a suspension of red blood cells in isotonic saline solution on a slide which is allowed to stand for one hour before making a reading. The fluid, after removal from the refrigerator, should be placed in a bath of lukewarm water. Hot water should not be used, as coagulation of the proteins of the fluid at the circumference of the flask may occur, rseulting in a post-transfusion reaction. Before use, the fluid should be filtered through fifteen layers of gauze. It should be administered by vein in the customary manner of transfusion.

It might be pertinent at this point to review briefly the results of ascitic fluid transfusion in animals suffering from hemorrhagic shock. Dogs weighing from 7 to 10 Kg. and anesthetized with pentobarbital sodium in appropriate amounts were used. Shock was considered to be present when sufficient blood had been removed to reduce the blood pressure to or below 60 mm. of mercury. The amount of blood removed varied from 3.4 to 5.2 per cent of the body weight. By transfusing human ascitic fluid it was possible to raise the blood pressure from the shock level and to maintain it at a normal level. The animals made a good recovery. There was no evidence of albuminuria, which suggests that the proteins of the ascitic fluid were retained by the animal. Illustrative data are shown (charts 4 and 5). It should be stated that preliminary cross-matching tests were carried out between the ascitic fluid and the blood of the prospective recipient.

The next step was to determine the availability of the fluid for human beings. At the time of writing, 22 transfusions with ascitic fluid have been performed, details of which will be given elsewhere. In a previous communication it has been shown that ascitic fluid is nontoxic and may be administered in large amounts intravenously (Davis and Blalock[109]). Despite the fact that ascitic fluid contains no hemoglobin, its use in states associated with acute loss of whole blood is rational, as in such states there is usually enough hemoglobin remaining to carry on the

110. Weil, P., and Isch-Wall, P.: Hémo-agglutinines des divers liquides organiques, Compt. rend. Soc. de biol. **88**:173-175, 1923.

111. Yosida, K. I.: Ueber die gruppenspezifischen Unterschiede der Transsudate, Exsudate, Sekrete, Exkrete, Organextrakte und Organzellen des Menschen und ihre rechtsmedizinischen Anwendungen, Ztschr. f. d. ges. exper. Med. **63**:331-339, 1928.

112. Schiff, F.: Ueber die gruppenspezifischen Substanzen des menschlichen Körpers, Jena, Gustav Fischer, 1931, p. 71.

respiratory functions of the blood. Only 3 Gm. of hemoglobin per hundred cubic centimeters of blood is necessary to maintain adequate oxygenation in the mammalian organism.

A further step in this study was the concentration of ascitic fluid and its preservation in a lyophile form. Ascitic fluid was lyophilized

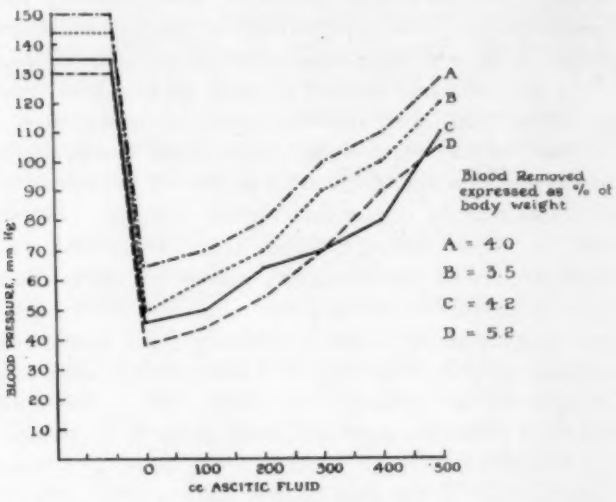

Chart 4.—Influence of ascitic fluid transfusion in cases of experimental hemorrhagic shock.

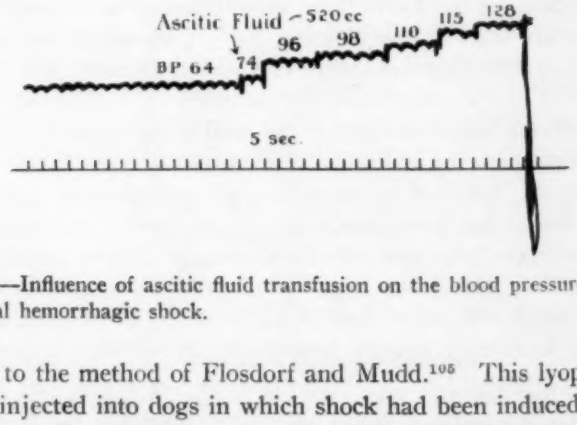

Chart 5.—Influence of ascitic fluid transfusion on the blood pressure in cases of experimental hemorrhagic shock.

according to the method of Flosdorf and Mudd.[105] This lyophile ascitic fluid was injected into dogs in which shock had been induced by graded hemorrhage. The blood pressure and the metabolic rate, which had fallen, were elevated to normal levels, where they were maintained (Mulder, Davis and Streeter [113]).

113. Mulder, A. G.; Davis, H. A., and Streeter, A.: On the Use of Dried (Lyophile) Ascitic Fluid in Hemorrhagic Shock, Am. J. Physiol. **126**:588-589, 1939.

LOSS OF PLASMA

States associated with loss of plasma or plasma-like fluid from the blood stream present peculiar therapeutic problems and, therefore, merit separate consideration. In order to clarify this discussion, one may regard plasma as a mixture of proteins and water. Loss of either the protein or the aqueous fraction, or of both, may occur, and this loss may be acute or chronic. The different forms of plasma loss and their causes are given (table 2).

Physiologic Effects of Loss of Plasma.—The effects of loss of plasma are dependent on two facts: (1) the rate of loss and (2) the nature

TABLE 2.—*Forms of Loss of Plasma*

Rapidity of Loss	Fraction Lost	Etiologic Factors	
		Experimental	Clinical
Acute	Aqueous	Subcutaneous injection of hypertonic sodium chloride solution (Davis)	Acute dehydration due to excessive perspiration, vomiting or diarrhea
Chronic	Aqueous	Water deprivation	Chronic dehydration due to excessive loss or insufficient intake of water
Acute	Protein and Aqueous	1. Burns 2. Freezing 3. Intraperitoneal and subcutaneous injection of bile 4. Prolonged application of constrictor to extremity 5. Trauma 6. Manipulation of bowel 7. Tissue autolysis in vivo	Burns Bile peritonitis Freezing Strangulation of bowel Mesenteric obstruction Acute pancreatitis Trauma
Acute	Protein	Plasmapheresis	None
Chronic	Protein	Plasmapheresis Low protein diets	Nutritional edema Surgical hypoproteinemias

of the fraction lost. Acute loss of either the aqueous or the protein fraction or of both results in reduction of the plasma volume, increased concentration of the red blood cells and hemoglobin, reduction of the oxygen content of the blood and increase in the carbon dioxide content. Clinically, the evidences of secondary shock manifest themselves. Chronic loss of the plasma fractions does not usually lead to shock. Loss of the aqueous portion of the plasma has already been considered in the discussion of dehydration. Chronic depletion of the protein fraction leads to reduction of the osmotic pressure of the blood, resulting in a disturbance of water balance. Edema of the skin and of the viscera and serous transudates may appear. Reduction of the total blood volume and hemoconcentration are absent with this form of loss of plasma. Disturbances in the motility of the gastrointestinal tract have been observed in association with diminution of the protein frac-

tion of the plasma (Barden, Ravdin and Frazier [114]). Hypoproteinemia in surgical patients, which is usually due to a variety of factors, such as insufficient protein intake, infection, loss of protein by drainage, hemorrhage before or during operation and deficient protein synthesis (Jones and Eaton;[115] Curphey and Orr [116]), may also lead to delayed wound healing and even to wound disruption (Thompson, Ravdin and Frank [117]).

Measurement of Degree of Plasma Loss.—The extent and type of loss of plasma may be measured directly or indirectly. Direct determination of the plasma volume may be carried out by the various dye methods, of which Gregersen and Gibson's [118] is probably the most accurate. Indirect determinations will reveal hemoconcentration with

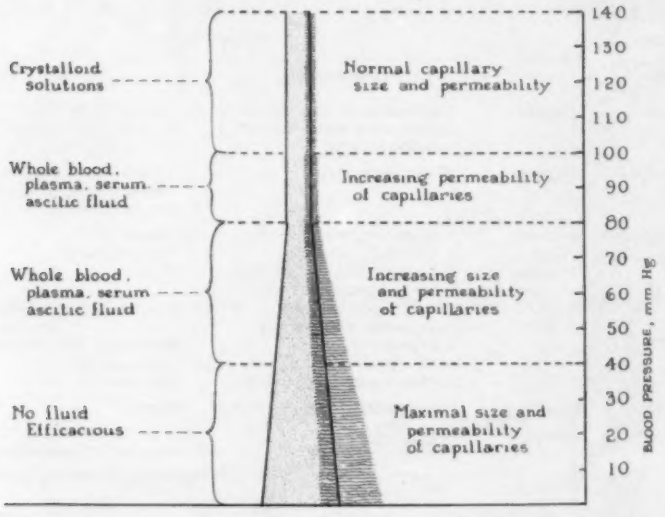

Chart 6.—Shock due to loss of plasma; efficacy of replacement fluids in relation to capillary permeability.

normal or slightly lower concentration of plasma protein when acute loss of the protein and aqueous fractions of the plasma has occurred.

114. Barden, R. P.; Ravdin, I. S., and Frazier, W. D.: Hypoproteinemia as a Factor in the Retardation of Gastric Emptying After Operations of the Billroth I and II Types, Am. J. Roentgenol. **38**:196-202, 1937.

115. Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema, Arch. Surg. **27**:159-177 (July) 1933.

116. Curphey, W. C., and Orr, T. G.: Edema in Surgical Patients, Surgery **1**:589-594, 1937.

117. Thompson, W. D.; Ravdin, I. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption, Arch. Surg. **36**:500-508 (March) 1938.

118. Gregersen, M. I., and Gibson, J. G.: Conditions Affecting Absorption Spectra of Vital Dyes in Plasma, Am. J. Physiol. **120**:494-513, 1937.

When the aqueous fraction alone has been lost, the hemoconcentration will be accompanied with an increased concentration of the plasma proteins. In the presence of chronic loss of the protein fraction the erythrocytes and hemoglobin are normal or diminished in amount, but the level of plasma protein, of course, is lowered.

Fluid Replacement.—Reduction of the plasma volume due to dehydration will not be reconsidered in the following discussion. In cases of acute loss of plasma with hemoconcentration and its sequelae, the crux of the therapeutic problem is the institution of fluid replacement before the capillary walls have been irreversibly damaged by oxygen lack (chart 6). Crystalloid solutions should be used with caution, are often ineffective and may actually reduce the plasma proteins still further by washing them out of the blood stream into the interstitial tissue spaces, the peritoneal cavity and the site of trauma (Beard and Blalock;[54] Davis [55]). Acacia solutions likewise are contraindicated, for two reasons: 1. Such solutions may interfere with the respiratory functions of the blood by coating the red blood cells. 2. They may adversely affect regeneration of plasma protein by the liver. The presence of hemoconcentration and increased viscosity of the blood would suggest that solutions of normal human proteins without red blood cells might prove more effective than whole blood. Such solutions are plasma, serum and human ascitic fluid. Although ascitic fluid has a somewhat lower protein content than either plasma or serum, it is usually available in larger quantities, and as much as 2,500 cc. may be given during twenty-four hours. If dehydration complicates the acute loss of plasma, crystalloid solutions may be given, but only after the plasma volume has been restored by protein-containing solutions. It is important to remember that the level of the blood pressure is no indication of the degree of loss of plasma. By the time the blood pressure has reached the accepted "shock" level (80 mm. of mercury), a considerable loss of plasma has occurred, and there are present a severe degree of oxygen lack and an increased permeability of the capillaries. A more reliable prognostic index is the level of hemoconcentration, but this, too, may be misleading if dehydration or loss of whole blood is superimposed on the loss of plasma. The most trustworthy criterion of circulatory deficiency associated with acute loss of plasma is the level of oxygen saturation of the blood. Determination of the potassium content of the blood as an index of the severity of shock has not proved reliable in our hands. The dangers connected with administration of crystalloid solution in the presence of conditions associated with reduction of the plasma volume are illustrated by the following 2 cases.

Case 2.—A white girl aged 13 years was admitted to the Charity Hospital suffering from first and second degree burns of the left arm, right axilla, back and abdomen. Each day 2,000 to 3,000 cc. of 5 per cent dextrose in isotonic

saline solution was administered by vein. The blood pressure gradually fell, and the patient died five days after admission to the hospital. Autopsy revealed extreme edema of the subcutaneous tissues of the entire body, which, when incised, released large amounts of straw-colored fluid. The pleural cavities each contained 300 cc. of clear straw-colored fluid. The pericardial cavity contained an excess of fluid. The lungs were voluminous and frothy on section, and microscopic examination revealed pulmonary edema. Other observations were hemorrhage into the left adrenal gland, fatty metamorphosis of the liver and extreme distention of the mucosal capillaries of the gastrointestinal tract.

The water-logging of the tissues, the bilateral hydrothorax and the pulmonary edema probably hastened the circulatory failure in this patient. Trusler and his co-workers[119] stated the belief that water intoxication may follow the excessive administration of fluids to patients suffering from shock due to burns. The reduction of the total plasma volume will not be revealed by simple determination of the level of serum protein. If an effort is made to replace the plasma which has been lost by administering solutions containing proteins, preferably of human origin, the subsequent use of crystalloid solutions is less likely to be attended with untoward results. Case 3 confirms this statement.

Case 3.—A white man aged 24 years was admitted to the Charity Hospital suffering from first and second degree burns of the face, neck, trunk and upper extremities, resulting from the explosion of a kerosene stove. The blood pressure was 120 systolic and 80 diastolic and remained stable. On the first day, 3,000 cc. of 10 per cent dextrose in isotonic saline solution was given by vein. On the second day, another 1,000 cc. of the same solution was administered. The condition of the patient was not good. The total amount of urine secreted in the first forty-eight hours was 500 cc. On the third day, because of the low output of urine, another 1,000 cc. of 10 per cent dextrose in isotonic saline solution was given by vein. The patient's face and body were now edematous. The value for serum proteins was 5.5 Gm., that for albumin 4.3 Gm. and that for globulin 1.2 Gm. per hundred cubic centimeters. The patient was seen by one of us (H. A. D.) on the evening of the third day, and an ascitic fluid transfusion was decided on. Accordingly, 475 cc. of group-compatible human ascitic fluid was given by the intravenous route at a rate of 5 cc. per minute. A brisk diuresis occurred during the transfusion. The following day the edema of the face and body had disappeared, and the output of urine was considerably increased. On the fifth day after admission, the level of serum protein had risen to 6.8 Gm. per hundred cubic centimeters. The patient made an excellent recovery, without recurrent edema of the face or of the body.

The therapeutic problem in cases of chronic loss of the protein fraction of the plasma is not prevention of secondary shock but correction of the disturbance of distribution of the body fluids resulting from lowering of the osmotic pressure of the blood. It is apparent that only protein-containing fluids, such as whole blood, plasma, serum and

119. Trusler, H. M.; Egbert, H. L., and Williams, H. S.: Burn Shock: The Question of Water Intoxication as a Complicating Factor, J. A. M. A. **113**:2207-2213 (Dec. 16) 1939.

ascitic fluid, are indicated. It should be pointed out that in treating hypoproteinemia with ascitic fluid transfusions it is not necessary to limit the amount of fluid transfused to 500 cc. As much as 2,500 cc. of ascitic fluid may be transfused during a period of twenty-four hours. Lyophile plasma has been utilized in such hypoproteinemic states, but post-transfusion reactions have been severe (Thompson, Ravdin, Rhoads and Frank [120]). Acacia solutions are contraindicated because of their proved deleterious action on protein regeneration. Elman and Weiner [121] have recommended the use of intravenous fluids containing amino acid mixtures. Finally, the danger of intravenous hypertonic and even isotonic solutions of sodium chloride should be kept in mind when hypoproteinemia is present. Edema of the body tissues may be precipitated, due to fixation of the sodium chloride and water in the tissues. Such "salt" edemas are apt to resist treatment. The use of desoxycorticosterone acetate is contraindicated.

CONCLUSIONS AND SUMMARY

Fluid replacement in various surgical states associated with a reduction of the water, electrolyte, blood and plasma content of the body is considered. Such replacement must be based on an understanding of the underlying disturbances of body function. The experimental and clinical aspects of ascitic fluid transfusion are discussed.

NOTE.—Since this paper was submitted for publication, we have transfused into human beings ascitic fluid which preliminary cross-matching tests had revealed to be incompatible with the blood of the prospective recipient. No reactions occurred. This will be discussed in more detail in a forthcoming paper.[122]

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120. Thompson, W. D.; Ravdin, I. S.; Rhoads, J. E., and Frank, I. L.: Use of Lyophile Plasma in Correction of Hypoproteinemia and Prevention of Wound Disruption, Arch. Surg. **36**:509-518 (March) 1938.

121. Elman, R., and Weiner, D. O.: Intravenous Alimentation with Special Reference to Protein (Amino Acid) Metabolism, J. A. M. A. **112**:796-802 (March 4) 1939.

122. Davis, H. A.: The Inactivation of Group-Specific Isoagglutinins in Relation to the Transfusion of Incompatible Plasma, Serum and Ascitic Fluid, to be published.

IMPROVEMENT IN BLOOD TRANSFUSION SERVICE

II. ESTABLISHMENT AND OPERATION OF A BLOOD TRANSFUSION SERVICE

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CINCINNATI

The selection and artificial preparation of high-titered test serums, the study of the cause and prevention of hemolytic transfusion reactions, the consideration of the role of subgroups and intragroup agglutinins in transfusion accidents, and the adoption of a simple, accurate technic for determination of blood grouping and compatibility have been described. All are parallel actions directed toward a single purpose, the transfusion of blood with the greatest simplicity and the least possible delay in laboratory procedure, with observance of the best known standards of safety.

Another major obstacle to the dispatch of blood transfusion service in large municipal hospitals is the inaccessibility of blood donors. There are delays, inefficiency and tragic results attendant to location of friends and relatives and the laboratory search for compatible and suitable bloods for patients whose bloods are of the rare groups. Occasionally, there is an emergency which does not permit even the time used to select a donor for a patient whose blood is of the common group. These are matters of ordinary knowledge to any resident physician. Any innovation in blood transfusion service which abolishes these delays results in a decreased morbidity and the saving of lives. It becomes another, parallel force designed to accomplish the same purpose as the technical improvements and considerations mentioned.

Such an innovation is the establishment of the American Red Cross Blood Transfusion Service at the Cincinnati General Hospital. This service consists of a blood bank and a volunteer donor bureau. In this paper will be presented the details of organization and method of operation of this service. A statistical analysis of the first 3,077 transfusions of refrigerated blood will follow.

EARLY INVESTIGATION

Although a few experimental works were recorded earlier in this century, the widespread clinical use of preserved blood is strictly a

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development belonging to the past decade. Rous and Turner,[1] of the Rockefeller Institute, preserved blood by adding an anticoagulant medium consisting of two parts of isotonic sodium citrate solution and five parts of isotonic dextrose solution to three parts of whole blood. They were chiefly interested in red blood cells and noted that in this mixture the cells remained intact for four weeks. Their only attempts at transfusion were experimental and were limited to the transfusion into animals of red blood cells suspended in physiologic solution of sodium chloride, the plasma having been discarded. The first recorded transfusion of preserved whole blood was that of Weil.[2] Blood from three to five days old, to each 10 cc. of which 1 cc. of 10 per cent sodium citrate solution had been added, was transfused. During the World War Robertson[3] employed the Rous-Turner technic in 20 cases. The red cells of blood which had been stored for as long as twenty-four days were given intravenously after suspension in isotonic salt solution. The plasma was discarded because of fear of too high a concentration of sodium citrate in the whole blood mixture. Interest lagged in this investigation for a number of years after the World War, but it received considerable encouragement when Yudin,[4] of Moscow, Russia, reported the results in 1,000 transfusions of refrigerated cadaver blood. Added impetus also emanated from Russia as a result of reports of the transfusion of preserved blood obtained from the placental end of the severed umbilical cord. The transfusion of placental blood was first reported from this continent by Goodall.[5]

At the Cincinnati General Hospital, use of the cadaver as a source of blood was investigated only from the standpoints of obtaining the blood in sterile culture and of determining how much blood could be obtained. Before blood was drawn from the cadaver, the following requirements had to be met:

1. It was necessary to obtain an autopsy permit and to draw the blood within six hours after death, since the danger of penetration of intestinal bacteria into the blood stream after six hours is great.

2. It was necessary to predetermine that no infectious disease was present at the time of death.

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1. Rous, P., and Turner, J. R.: Preservation of Living Red Cells in Vitro, J. Exper. Med. **23**:219, 1916.

2. Weil, R.: Sodium Citrate in the Transfusion of Blood, J. A. M. A. **64**:425 (Jan. 30) 1915.

3. Robertson, O. H.: Transfusion with Preserved Red Blood Cells, Brit. M. J. **1**:691, 1918.

4. Yudin, S. S.: Transfusion of Stored Cadaver Blood: Practical Considerations; the First Thousand Cases, Lancet **2**:361, 1937.

5. Goodall, J. P.; Anderson, F. O.; Altimas, G. T., and McPhail, F. L.: Inexhaustible Source of Blood for Transfusion and Its Preservation, Surg., Gynec. & Obst. **66**:176, 1938.

3. Freedom from syphilis as determined by previous negative Wassermann or Kahn reactions was necessary.

Once these requirements were met it was found that only 1 cadaver each three or four weeks was available for extraction of blood. The average amount obtained from each of 3 cadavers by cannulating the internal jugular vein with the head in a dependent position was 1,200 cc. Efforts toward obtaining blood from this source were abandoned because the amount obtainable was too small to be of value to a transfusion service which required approximately 4,000 cc. of blood per day and also because it was believed that patients would not be willing to accept the transfusion of blood from a cadaver.

With the technic outlined by Goodall and in cooperation with the obstetric department, fetal cord blood as a source of supply was investigated. Quantities obtained in sterile culture amounted to about 115 cc. for each cord. The available cords for which negative Wassermann reactions could be obtained averaged six each day. Thus six operations and six sets of sterile equipment were required in order to obtain less than 700 cc. of blood. The pooling of these bloods in order to obtain amounts for practical use and the number of grouping tests required in the laboratory before they could be pooled were added difficulties. The experience in this clinic is that an equal amount of blood can be obtained with much less difficulty from friends and relatives and from other volunteer donors. For this reason, placental blood obtained from fetal cords is regarded here as an impractical source of supply.

The problem which confronts a large hospital with a busy transfusion service is not the source of the blood but rather the need for a reserve supply which will eliminate delay in cases of emergency and which can be depended on so that elective transfusions may be scheduled in advance for purposes of expediency. For this reason it is probably true that the outstanding contribution resulting from the transfusion of preserved cadaver and placental blood has been to make physicians connected with the blood transfusion services in large hospitals conscious of the fact that blood from ordinary donors can be drawn in advance and preserved and the supply replenished whenever the opportunity affords, with creation of a constant supply of blood which can be depended on to absorb delays incident to either emergency or elective transfusions.

As an outgrowth of this consciousness, blood banks are now operating in several hundred hospitals in the United States. The first one was established at the Cook County Hospital in Chicago in 1937.[6] Others are maintained at the University of Pennsylvania Hospital, the Phila-

6. Fantus, B.: The Therapy of the Cook County Hospital: Blood Preservation Technic, J. A. M. A. **111**:317 (July 23) 1938.

delphia General Hospital, the Presbyterian Hospital, New York City, the New York Hospital, the Los Angeles County Hospital and the Cincinnati General Hospital.

PRESENT STATUS OF BANK BLOOD

Blood is a living fluid, and the limitations of its use when preserved have become a problem of major interest. In the short space of two years much work has been done in various clinics in order to answer the natural questions which arise pertaining to these limitations. The question of how long blood can be stored before use can be answered only by further study of the changes which occur in the many different components desirable in transfusions. When the stability of each of these components has been determined and is known in terms of days, the answer to the question of how long blood may be kept before transfusion will be known. The length of time will undoubtedly vary a great deal, depending on what component of the blood is desired for a particular transfusion. The only two methods of approach for this study are: (1) determination of the changes which occur in preserved blood and (2) evaluation of the results of transfusion of such blood.

In regard to the changes which occur in preserved blood, the following contributions are of interest. Using Kjeldahl nitrogen determinations on properly refrigerated blood as indexes of proteolysis, Kremerman [7] concluded that blood stored for twenty-one days is not toxic to the recipient as far as the degree of proteolysis is concerned. Scudder [8] observed a shift of potassium ions from cells to plasma and stated that care should be taken in using it in certain types of cases. It seems doubtful, however, that the amount of free potassium is sufficient to cause toxic symptoms.

The marked hemolysis of red cells which occurs at the end of ten days has been a subject of much discussion, since erythrocytes are the important elements in the treatment of hemorrhage and anemia. Following the lead offered by the early work of Rous and Turner, DeGowin [9] has shown that the addition of 13 parts of 5.4 per cent of dextrose solution and 2 parts of 3.2 per cent of sodium citrate solution to each 10 parts of blood prevents rapid hemolysis and delays diffusion of the potassium ion into the serum. It is obvious, however, that this mixture should not be added routinely to all bank blood, since the dilu-

7. Kremerman, R. B.: Med. eksper., November 1938, p. 29.

8. Scudder, J.; Drew, C. R.; Corcoran, D. R., and Bull, D. C.: Studies in Blood Preservation: I. Repartition of Potassium in Cells and Plasma, J. A. M. A. **112**:2263 (June 3) 1939.

9. De Gowin, E. L.; Harris, J. E., and Plass, E. D.: Changes in Blood Preserved for Transfusion, Proc. Soc. Exper. Biol. & Med. **50**:126, 1939.

tion would reduce the blood efficiency of the fluid transfused to 40 per cent per unit volume. The result of DeGowin's work may find practical application in those cases in which the volume of fluid transfused can be raised to the point desired without contraindication. Certainly in the treatment of shock, in which the plasma is the desired element and the erythrocytes are generally considered inconsequential, any dilution of bank blood is undesirable, because of the diminution in the hydroscopic action of the plasma which results.

Rhoads and Panzer [10] stated the belief that bank blood is an unsatisfactory source of plasma prothrombin for treatment of the hemorrhagic diathesis associated with jaundice. They based their opinions on determination of the prothrombin time of bank blood plasma by the method of Quick.[11] Lord and Pastore [12] made the same study on bank blood, using the method of Warner, Brinkhous and Smith [13] as well as the method of Quick. They corroborated the work of Rhoads and Panzer by the method of Quick but showed that the prothrombin level dropped only to 84 per cent in eight days as compared with 23 per cent by the Quick test with the method of Warner, Brinkhous and Smith. At the end of twelve days the prothrombin time was 27 per cent by the method of Quick and 75 per cent by the method of Warner, Brinkhous and Smith. These data were on properly refrigerated blood (2 to 4 C.). Determinations made by Lord and Pastore on the prothrombin time of plasma kept at ordinary ice box temperature showed the prothrombin time to be only 48 per cent in twelve days (method of Warner, Brinkhous and Smith). The discrepancy in the results obtained with use of the method of Warner, Brinkhous and Smith as compared with those obtained by the method of Quick was partially explained by Lord and Pastore by the fact that the quick test controls only the calcium and thromboplastin (since Quick correctly considered it unimportant to control the fibrinogen content, which is normal in the blood of the jaundiced patient) and that the Warner, Brinkhous and Smith test controls the fibrinogen as well. Since the difference in the level in the prothrombin time of bank blood when determined by the two methods is created by the addition of fibrinogen and since the fibrinogen content of

10. Rhoads, J. E., and Panzer, L. M.: The Prothrombin Time of "Bank Blood," J. A. M. A. **112**:309 (Jan. 28) 1939.

11. Quick, A. J.: The Nature of the Bleeding in Jaundice, J. A. M. A. **110**: 1658 (May 14) 1938.

12. Lord, J. W., and Pastore, J. B.: Prothrombin Content of Bank Blood, J. A. M. A. **112**:309 (Jan. 28) 1939.

13. Warner, E. D.; Brinkhouse, K. M., and Smith, H. P.: A Quantitative Study on Blood Clotting: Prothrombin Fluctuations Under Experimental Conditions, Am. J. Physiol. **114**:667, 1936.

bank blood plasma has been shown by Bancroft [14] to be normal quantitatively, a possible explanation of the difference in results may lie in the fact that there are qualitative changes in the fibrinogen of bank blood plasma. However this may be, Lord and Pastore concluded that bank blood is an adequate source of plasma prothrombin for about nine days, as determined by the accurate method of Warner, Brinkhous and Smith. They also concluded that carefully controlled refrigeration is an important factor in the preservation of prothrombin. Their conclusions are reasonable, and, since the fibrinogen content of the plasma in jaundiced patients is quite normal, the prothrombin which is transfused should be affected by the fibrinogen of the patient in such a manner as to decrease the clotting time, just as occurs when the fibrinogen is added in a test tube according to the method of Warner, Brinkhous and Smith. A carefully controlled study of the effects of bank blood of various ages on the prothrombin time of patients with jaundice has never been made and would be of extreme value at present in order to determine this particular limitation of bank blood.

Another question of interest as to the limitations of bank blood is that of sterility. Reports showing the results of culture of specimens taken from bank blood are too numerous to mention. It is generally agreed that, provided careful technic is exercised in the drawing of the blood in a closed system, it is not desirable routinely to culture bank blood before it is transfused. The mere taking of the sample for culture subjects the specimen to increased opportunity for contamination. Novak [15] concluded that pyrogens produced by bacteria growing in bank blood may be a cause of transfusion reactions and stated that the frequency of transfusion reactions with bank blood "ranges up to 50 per cent depending on the index used for defining a transfusion reaction." He did not say where these statistics were obtained. Assuming that the lack of sterility is a major cause of transfusion reactions, Novak advocated the addition of sulfanilamide, 20 mg. per hundred cubic centimeters of blood, as a bacteriostatic agent. His method was to inoculate 10 cc. of fresh blood with twenty-four hour cultures of Staphylococcus albus, Pseudomonas aeruginosa and hemolytic spore-forming rods. The specimens were then plated on agar, and the colonies were counted after refrigeration for forty-eight hours at 4 to 6 C. Complete bacteriostasis and in some cases sterilization were effected by a concentration of sulfanilamide of 20 mg. per hundred cubic centimeters. It is doubtful that pyrogens produced by bacteria growing in bank blood drawn with proper sterile technic are a cause of transfusion reactions, since the

14. Bancroft, F. W.; Stanley-Brown, J., and Quick, A. J.: Post Operative Thrombosis and Embolism, Am. J. Surg. **28**:648-668, 1935.

15. Novak, M.: Preservation of Stored Blood with Sulfanilamide, J. A. M. A. **113**:2227 (Dec. 16) 1939.

incidence of reactions in some reported series of bank blood transfusions is no greater than the incidence of reactions in reported series of transfusions of fresh blood.

Drew and Scudder [16] carefully determined the fate of thrombocytes in bank blood and found that they rapidly fall to less than 100,000 for each cubic millimeter in twenty-four hours and to 40,000 at the end of three days. Kolmer [17] also demonstrated the instability of platelets. Because of this, bank blood should not be used as a source of thrombocytes.

Numerous workers [18] have demonstrated the degree of spontaneous hemolysis in properly refrigerated bank blood. The results of their studies indicate that preserved blood is a good source of erythrocytes up to five days and should not be used for this purpose after eight days.

The age limitation that should be placed on preserved blood which is used in the treatment of infections, septic states and septicemias is not yet clear and must necessarily depend on the component or components of blood desired in a particular case. The supportive value of the elements contained in plasma for nutrition and of the red cells in combating the anemia associated with these conditions is well known. Since the value of immune substances, both specific (antibodies) and nonspecific bactericidal (leukins and plakins), even in fresh blood in 200 to 500 cc. amounts is debatable, deterioration of these substances in preserved blood as shown by Kolmer [17] may or may not be a limitation to its use. Observations made during his studies on citrated blood preserved at 4 to 6 C. were as follows:

1. Complement is well preserved up to fourteen days.

2. Bactericidal activity for Staphylococcus aureus, the beta hemolytic streptococcus and Bacillus coli is decreased after seven days' preservation.

3. The phagocytic activity of neutrophils on the same three organisms is definitely reduced within seventy-two hours, becoming markedly so about the fifth day owing to degenerative changes in the leukocytes.

4. The leukocytes display degenerative changes within twenty-four hours.

5. The platelets exhibit distinct clumping immediately, with evidence of deterioration in twenty-four hours. They are scarce at the end of forty-eight hours.

16. Drew, C. R.; Edsall, K., and Scudder, J.: Studies in Blood Preservation, J. Lab. & Clin. Med. **25**:240, 1939.

17. Kolmer, J. A.: Preserved Citrated Blood "Banks" in Relation to Transfusion in Treatment of Disease with Special Reference to Immunologic Aspects, Am. J. M. Sc. **197**:442, 1939.

18. de Gowin, Harris and Plass.[9] Drew, Edsall and Scudder.[16] Kolmer.[17]

Although it is not established, Kolmer has stated the belief, as have many others, that immune substances in transfused blood are efficacious in the treatment of septic conditions and has concluded that fresh blood is preferable and that preserved blood more than 2 to 3 days old should not be used for these purposes.

The second method of approach to the study of the value of preserved blood, namely, the study of results of transfusion of such blood, is one which deserves careful attention and will increase in value as carefully compiled statistics accumulate. It is from this standpoint that the statistical analysis of 3,077 transfusions of refrigerated blood at the Cincinnati General Hospital becomes of interest. The results of this study are commented on as it is presented.

Schaefer and Wiener [19] traced the fate of the erythrocytes of bank blood after transfusion and found that the result when five to eight day

Age of Blood for Various Conditions

Condition of the Patient	Age of Blood in Days *
Shock not associated with toxemia (hemorrhagic, traumatic, surgical, thermal)	21
Anemia not associated with sepsis	8
Hypoproteinemia	21
Infection, septic state, septicemia	3
Hemorrhagic diathesis in obstructive jaundice	8
Thrombopenic purpura	½ (12 hrs.)

* The age limitations expressed above are maximum, and in actual practice almost all units of blood are issued several days before these time limits expire.

old blood was used was about the same as when fresh blood was transfused. The period of survival of the erythrocytes was from three to four months. However, four specimens of ten to twenty day old blood were transfused, and the erythrocytes given could not be demonstrated in the circulation of the recipient after from one to three weeks.

In the operation of the blood bank at the Cincinnati General Hospital it has been ordinary practice to dispense units of blood with regard to the known limitations of preserved blood for the particular cases, the age of the blood issued depending on the diagnosis submitted for the patient. Although it is constantly subject to change as more is learned concerning these limitations, a guide to the members of the house staff is posted at the time of this writing (see accompanying table). Experience of sixteen months' duration, during which time more than 3,500 transfusions of preserved blood have been given, has shown that these time limitations have not interfered with the practical operation of the blood bank service.

19. Schaefer, G., and Wiener, A. S.: Limitations in the Use of Preserved Blood for Transfusions, Quart. Bull., Sea View Hosp. **5**:17, 1939.

ORGANIZATION OF THE SERVICE

The American Red Cross Blood Transfusion Service, consisting of a blood bank and a volunteer donor bureau with headquarters at the Cincinnati General Hospital, is the first of its kind. It is without precedent that a local chapter of the American Red Cross has collaborated with a municipal hospital in order to produce such an organization. The Cincinnati and Hamilton County Chapter of the American Red Cross first became interested in a service to be offered all hospitals and physicians in Hamilton County early in 1938. In May 1938 the officials of the Red Cross, in order to ascertain whether such a service was badly needed, met with a group consisting of physicians, superintendents of Cincinnati Hospitals, members of the Hamilton County Board of Health and representatives of industrial hospitals. A plan of operation was proposed at this time and was given unqualified approval by all members of this group. On the basis of this assurance, the Red Cross was willing to proceed with the financial support of the plan as outlined. The American Red Cross Blood Transfusion Service, with headquarters at the Cincinnati General Hospital, was then organized and has now been in full operation for more than a year. The administration, the headquarters, the physical equipment, the duties of the personnel and the method of operation of the service in relation to hospitals and physicians of Hamilton County are described in the following sections.

ADMINISTRATION OF THE SERVICE

The service is known as the American Red Cross Blood Transfusion Service. The medical direction and administration are responsibilities of a service committee appointed by the Cincinnati and Hamilton County Chapter of the American Red Cross, subject to the approval of the directing medical staff of the Cincinnati General Hospital. The interests of hospitals other than the Cincinnati General are represented by two memberships on this committee. There are a director and an assistant director of the service from the department of surgery at the Cincinnati General Hospital and the University of Cincinnati, who are also members of the service committee. This committee meets periodically to determine the policies of the service. The director or the assistant director is constantly available for normal operation.

HEADQUARTERS AND EQUIPMENT

The Cincinnati General Hospital provides space which measures 48 by 15 feet (14.6 by 4.5 meters) for the office, two booths for the drawing of blood and a laboratory and blood storage room. The hospital also furnishes water, janitor and laundry service, steam sterilization and electricity for lights, refrigeration and ventilation. Mechanical, carpentry and repair service are also partially maintained by the hospital. Items

of operating equipment, such as gauze sponges, cotton, towels, sheets, wrappers, rubber gloves, sterilizing solutions, hydrogen peroxide, iodine, procaine hydrochloride, sodium citrate, collodion, applicator sticks, cresol, ether, acetone and distilled water, are supplied at the expense of the hospital.

The Red Cross assumed the cost of physical changes in the space, including partitions, decorating, electrical wiring, light fixtures and plumbing. They also provided all fixed equipment for the office, booths and laboratory, and they supply all operating equipment not mentioned. The office equipment includes desks, chairs, filing and storage cabinets, one typewriter, office supplies and printed forms. Each booth is equipped with a donor bed, two utility tables and auxiliary lights. The laboratory equipment, purchased and supplied by the Red Cross, includes one refrigerator, the laboratory desk and sink, storage cabinets for linen and sterile supplies, one microscope, one drying oven, human blood grouping

Items included in the donor set.

serums, glass slides, Petri dishes, glass pipets and platinum wire. The Red Cross also furnishes the items used in the donor sets with the exception of the muslin wrappers, gauze and powder paper. These items are as follows: One 28 by 28 inch (71 by 71 cm.) wrapper, one aluminum container, one 24 by 24 inch (61 by 61 cm.) wrapper, one 14 by 14 inch (35.5 by 35.5 cm.) wrapper, two test tubes stoppered with cotton, one hypodermic syringe, two gauze flask covers with powder paper folded inside, one gauze pad with 13, 15 and 25 gage needles with stilets inserted, one 750 cc. graduated Erlenmeyer flask, one two-holed rubber stopper with glass bends and rubber tubing attached and one metal adaptor (see accompanying illustration).

PERSONNEL

The salaried personnel of the service consists of three laboratory technicians and a secretary. Their salaries are paid by the Red Cross. The technicians operate in three eight hour shifts, covering the entire

twenty-four hours of each day. Each is relieved for one day each week by a senior medical student provided by the National Youth Administration.

METHOD OF OPERATION

Early in the conception of this service it was considered highly desirable to incorporate into the service headquarters all the activities possible pertaining to the transfusion of blood. Reactions which result from the transfusion of blood are known to be caused by a multiplicity of factors, which may be due either to improper technic used in the drawing of blood or to careless handling and cleansing of the equipment which comes into contact with the blood, as well as to errors made in the laboratory testing of blood prior to transfusion. All these activities are carried out at central headquarters in order to avoid deviations from acceptable standards of technic, which would be uncontrollable if facilities were scattered and responsibility divided. Also, under a system of centralized control special problems relative to the known limitations of bank blood can best be met, and improvements in technic pertaining to any of the aforementioned procedures can be readily adopted and enforced. Too much emphasis cannot be placed on these considerations. A properly regulated blood bank should result in a decreased incidence of transfusion reactions, and it must consist of more than a refrigerator in which to store blood.

The blood transfusion service consists of two almost independent divisions, a blood bank and a volunteer donor bureau, operating under the same direction from the service headquarters. The operation of these divisions will be described separately.

1. *The Blood Bank.*—The house physician desiring blood for transfusion presents a small sample of defibrinated whole blood from the patient to the office, together with a request form bearing the date, the name of the physician, the service, the ward, the patient's name, the case number, the race of the patient, the diagnosis and the time the blood is desired. If for some reason relatively fresh blood is indicated, the maximum age possible is recorded on the request form. The technician, after determining the group of the blood sample, makes a direct match with a sample carried on the side of a unit (500 cc.) of blood of the same group from the refrigerator. If blood of the identical group is not available, group O bank blood is matched against samples of group A or B, and group A or B bank blood is matched against samples of group AB. The entire laboratory procedure requires twenty minutes, and in cases of extreme emergency the blood is issued in five minutes, pending the result of the direct match. This result is then relayed by telephone, which allows the physician to utilize the fifteen minutes required for the direct match in dispensing with all preparations preliminary to the

actual transfusion. To a tag form which is carried on the bottle of refrigerated blood issued is added the name of the patient, and this is filed alphabetically, according to his name. This file then becomes of value in determining the number of transfusions given to any patient and the identity of the donors.

For each withdrawal of 500 cc. of blood the secretary enters the data contained on the request form, the age of the blood issued and one debit unit in the monthly record of transactions. Each hospital service, such as medicine, general surgery, gynecology or obstetrics, is held responsible for a balance of its own debit and credit columns on this record. On the day following the transfusion the secretary makes a follow-up call to the responsible physician and records the presence or absence of a transfusion reaction. The total information compiled on the monthly record then becomes of value in the compilation of statistics for future study.

The replacement of a unit of blood which has been withdrawn becomes the obligation of the hospital service to which it was issued. In this way an obligation is not canceled when a physician who makes a withdrawal is transferred to another service or terminates his residency. Actual operation for more than a year has proved two important facts: first, that friends and relatives of patients and convalescent patients in whose cases there is no medical contraindication afford a more than adequate source of blood replacement and, second, that the bank will absorb without embarrassment reasonable delay, such as two to three days, in replacing a unit.

The physician presenting himself with a donor for replacement is expected to qualify the donor with a cursory medical history and physical examination. An accessible arm vein is required, because cutting down on a vein is not permitted. If these conditions are satisfied, the arm of the donor is draped and prepared for venipuncture by the technician while the physician scrubs. Preliminary grouping is not made unless there is an overstock or a shortage of one of the blood groups. The technician then assists the physician outside the sterile field in such matters as providing procaine hydrochloride, supplying sodium citrate for the flask, operation of the tourniquet, suction to the collecting system and collection of test tube samples of blood for future Kahn, grouping and matching tests.

The physician then assembles the donor set, injects 2 per cent procaine hydrochloride into the skin over the vein and, with the aid of the technician, adds 50 cc. of 2.5 per cent sodium citrate solution to the flask by suction through the collecting system. A 2.5 per cent sodium citrate solution is used in preference to a higher concentration in smaller volume in order to obtain better distribution of the solution throughout

the blood. Venipuncture is then made. The resulting per cent of sodium citrate (0.22) in the total volume (550 cc.) has proved to be sufficient to prevent any coagulation if the flask is almost constantly agitated by gentle rotation in alternate directions.

After 500 cc. of blood has been obtained, the rubber stopper and the contained glass bends are lifted from the flask before the venipuncture needle is withdrawn, and samples for Kahn tests and for grouping and matching are collected in the test tubes. The sterile cover, which consists of a powder paper and two layers of close-meshed muslin gauze filled with a layer of cotton sheet wadding, is then tied firmly over the neck and sides of the flask with gauze bandage.

At the end of the operation, entry is made in the credit column of the monthly record of transactions for the proper hospital service. The name of the donor is entered on the tag form which is attached to the flask's neck and on a form entitled "Donor of Bank Blood." The latter form is filed alphabetically according to the name of the donor and may be used in conjunction with the tag form in recalling him for a future transfusion in a case of protracted need. The test tube sample for future grouping and matching tests is labeled and placed in the metal container attached to the side of the flask. The sample for the Kahn test is labeled and placed with others for determination on the following morning.

The unit of blood is then placed on the "unclassified" shelf of the refrigerator and is removed to the "classified" shelf for the corresponding blood group after the blood group has been determined and a negative Kahn reaction has been obtained. In the event that the reaction is positive, a corroboratory Wassermann test is made. If the reactions to both tests are positive, the credit is withdrawn by drawing a red ink line through the entry on the monthly record. The physician is then notified of the cancelation, and a form letter is sent to the donor advising him of the need for treatment.

Once each month the names and addresses of all persons to whom this letter has been sent are submitted to the social hygiene council of the Public Health Federation for follow-up proceedings. During the past year over 300 persons having syphilis with no previous knowledge of the disease have been apprehended and directed to clinics or physicians for treatment. The value of this program as a collateral advantage to the community in the operation of the blood blank is obvious.

In addition to the performance of laboratory tests and assistance to the physician in drawing blood, the technicians are required to maintain proper equipment and tidiness in the donor booths, to make entries on printed forms in the absence of the secretary and mechanically to cleanse,

assemble and wrap donor sets preparatory to steam sterilization. Rigid adherence to the following procedure for preparation of items contained in the donor sets is maintained:

1. Flask
   (*a*) Scrub with a brush and tap water. Use 2 ounces (60 cc.) of hydrogen peroxide if necessary. (No other chemicals and no soaps are to be used.) Brushes used are never to touch soap or be used for any other purpose.
   (*b*) Irrigate with tap water over an inverted hydrant for three minutes by the clock.
   (*c*) Inspect closely for visible contaminants. Repeat *b* if contaminants are present. *Avoid handling the mouth of the flask from this step on.*
   (*d*) Rinse the inside of the flask thoroughly with 270 cc. of distilled water and invert the flask in the drying oven.
2. Rubber Tubing
   (*a*) All new rubber tubing introduced into a set must be boiled for fifteen minutes in 5 per cent sodium hydroxide solution.
   (*b*) Attach the tubes to a mechanical irrigator for five minutes. Repeat if visible contaminants are present.
   (*c*) Boil for fifteen minutes in 0.1 per cent sodium hydroxide solution.
   (*d*) Irrigate with tap water for two minutes.
   (*e*) Boil for five minutes in distilled water.
   (*f*) Shake well and place on the top shelf in the oven to dry.
3. Rubber Stoppers
   (*a*) All new stoppers introduced into sets must be boiled for fifteen minutes in 5 per cent sodium hydroxide solution.
   (*b*) Rinse thoroughly in tap water.
   (*c*) Same as 2 *c*.
   (*d*) Same as 2 *d*.
   (*e*) Boil for five minutes in distilled water, connect to right-angled glass tubes and place in oven to dry.
4. Glass Tubing
   (*a*) Attach to a mechanical irrigator for five minutes immediately after use.
   (*b*) Hold up to the light and inspect carefully for visible contaminants. Repeat step *a* and irrigate with hydrogen peroxide if contaminants are present.
   (*c*) Boil in distilled water for five minutes, and lay on a clean towel to dry.

5. Needles and Metal Adaptors
   (*a*) Scrub with hydrogen peroxide.
   (*b*) Irrigate with tap water.
   (*c*) Repeat *b* if contaminants are present.
   (*d*) Irrigate with distilled water.
   (*e*) Irrigate with 2 cc. of ether.

The laundering, steam sterilization and Kahn and Wassermann tests are the only operations performed outside the central quarters.

It is the duty of the technician to report any violation of sterile technic made in the drawing of blood to the director or assistant director of the service. The blood unit concerned is discarded, and the credit is withdrawn if a sterile culture is not obtained.

Each day an inventory of the units of blood of each group in the bank is recorded and filed. This information is of value in determining and anticipating an overstock or a shortage of any particular blood group in the bank. If an imbalance occurs, selective instead of random drawing of blood is exercised until it is corrected. This is done by determining the blood group of each prospective donor before drawing blood, rejecting donors of the group in which there is an overstock and selecting those of the group in which there is a shortage. Fortunately the volume of transfusions given by the service, an average of eight each day, is large enough to permit efficient operation most of the time without resort to selective drawing. It is our opinion that a blood bank would not be practicable for a hospital averaging less than five transfusions each day. To maintain an inventory of 50 units of blood, which is the least possible in order to secure a supply of the rarer blood groups, the average age of blood issued in a service requiring five transfusions a day would be ten days. The fluctuations in the supply resulting from ordinary delays in replacement in a service doing less in volume of transactions would result in periods of shortage of the rarer groups and overstocking with the commoner groups or vice versa. An overstock would require the waste of many bloods owing to age.

Because it is necessary to open the flasks in order to obtain specimens, which increases the opportunities for contamination, no effort is made to test units of bank blood for sterility.

The blood in the bank is maintained constantly at a temperature of from 2 to 4 C. Fluctuations in the temperature of the air inside the refrigerator caused by the necessary opening and closing of the doors is never more than 2 degrees (C.), as shown on recording thermometer charts.

Recordings of the temperature of the blood itself show no variation under the same conditions.

Separation of the blood from white and that from Negro donors in the bank has been a constant practice for reasons other than scientific ones. As is true in other phases of the practice of medicine, society is not yet willing to accept what medicine already knows. As far as is known, no immediate or ultimate undesirable effects accompany the transfusion of blood from a person with skin of one color to a person with skin of another.

2. *The Volunteer Donor Bureau.*—The volunteer donor bureau operates for the benefit of all hospitals in Hamilton County, not only the Cincinnati General Hospital. Early in the organization of the blood transfusion service it became obvious that major difficulties would be encountered if an attempt were made to extend the operation of blood banks to other hospitals. A unit of bank blood, if sent to a hospital at some distance away, must necessarily be replaced. This might be done by one of two methods. Either the replacement unit could be drawn at the hospital to which the unit was sent and returned by messenger to the bank, or the volunteer donor for replacement could be sent to the headquarters for the blood to be drawn there. The first method of replacement is highly undesirable, since it is impossible to control the technic under which blood is drawn unless it is done at central headquarters. The objection to the second method of replacement is that the service does not maintain a resident physician to draw blood. The only method of doing this would be to exploit the resident house staff at the Cincinnati General Hospital. Another objection to extension of the blood bank service to other hospitals is that the service is not anxious to usurp the functions properly belonging to a hospital relative either to the normally operating hospital procedure prior to transfusion or to the actual transfusion of blood. Instead, it desires to supplement these functions with a service which will make compatible and suitable blood quickly available whenever needed.

It is the experience of any hospital that in the majority of instances in which blood transfusion is desired the proper donor may be found among friends and relatives of the patient without undue delay. The volunteer donor bureau was organized as a second division of the Red Cross Blood Transfusion Service to serve all hospitals in Hamilton County when friends or relatives of the patient cannot be located or are not of the compatible blood group or when an emergency exists which does not permit waiting for laboratory search.

For this purpose the service maintains a list of certified blood donors which is available by telephone call day or night. The membership of this list was originally acquired through newspaper publicity. Its members are given a thorough physical examination. In addition, they are qualified each six months from the standpoints of age, good general health, negative Kahn reaction, absence of primary or secondary lesions of

syphilis, accessible arm veins and normal hemoglobin content of the blood. Periodic examinations are performed by volunteer physicians from the resident staff of the Cincinnati General Hospital. Each donor has expressed his willingness to respond at once to a service call, whether it be for an indigent patient or for one who is able to pay for the blood.

Each member of the list, when properly qualified, is issued a blood donor's identification book, which is his certificate of registration with the service. This book contains the signature of the donor, the date of registration and the registration number. In addition it contains a description of the donor, his blood classification, a record of the transfusions given through the service and a record of his periodic physical and laboratory examinations. The service maintains a card index in which each donor is classified according to blood group and the district in which he lives. The front of the card contains information necessary for quick communication with the donor. On the back of the card is a duplicate record of the results of periodic laboratory and physical examinations and of the transfusions given through the service.

With the permission of the Academy of Medicine of Cincinnati, each of its members and resident physicians of all hospitals in Cincinnati were acquainted with the operation of the service by means of a descriptive pamphlet. By telephone at any time, day or night, the physician may secure within an hour a volunteer donor of any blood group. The secretary or technician, on receiving the call, enters the necessary information on a printed form. The card index file of certified donors is then consulted, and a donor is selected with consideration for the following points: As far as possible the donors are used in rotation, in order that no one be asked to serve oftener than once each six weeks or to exceed four times each year and also that each donor is used often enough so that he retains his interest in the service. If the blood is needed for emergency use, a donor is called who lives close to the hospital. If the transfusion can be scheduled to meet the convenience of the donor, he is selected from an outlying district. Since all donor services are classified as to a "full pay," "part pay" or "indigent patient," an attempt is made also to distribute the "pay transfusions" throughout the list. Once the donor is selected, he is notified, and his name and the time of notification are recorded. A follow-up call to the physician from whom the request was received is made by the secretary on the next day. At this time the transfusion is credited to the donor on the back of his card in the index file.

Experience shows that to maintain a satisfactory list of donors it is necessary to give them every consideration to which they are entitled. For this reason the hospital staffs have been charged that the donor should be courteously received when he arrives at the hospital, that the blood should be drawn as promptly as possible and that he should be

dismissed with an expression of appreciation by the attending physician or nurse. They have also been asked not to call for a donor unless it is reasonably certain that he is to be used. After each transfusion the donor receives a letter of appreciation from headquarters.

When a call is received for a donor the person making the call is asked if the patient is indigent, "full pay" or "part pay." If the patient is indigent, no bill is sent. If he is classified as "full pay," the blood transfusion service sends a bill at the rate of $50 per 500 cc. of blood. A "part pay" patient is one who is able to pay something for the blood given but cannot afford to pay the full rate. In this case the amount of the payment is to be determined by the patient or his relatives. All statements are sent to the accounting department of the hospital for submission to the patient. It is undersood that the hospital is not responsible for collection of the money, its only function being submission of the bill. The hospital, however, is responsible for the payment of transportation of a donor to an indigent patient. Payment for all blood given is made by the patient to the service headquarters, and the sum is distributed at the rate of 80 per cent to the donor and 20 per cent to the service. Entry of financial details is then made.

Several reasons why the blood bank service could not be extended to hospitals other than the Cincinnati General Hospital have been stated. These objections would arise only if the sending of units of banked blood in response to requests for blood transfusion service were indiscriminate. If, however, in any instance of emergency the circumstances are such that the volunteer donor list service is not entirely adequate, bank blood is sent by taxicab. Such conditions are encountered only very occasionally, and the responsibility for replacement of these units in the bank is one that is readily and willingly met by the members of the resident staff of the Cincinnati General Hospital.

IMPROVEMENT IN BLOOD TRANSFUSION SERVICE

III. RESULTS OF 3,077 TRANSFUSIONS OF BANK BLOOD; A STATISTICAL ANALYSIS

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An important method of approach to the study of the value of preserved blood is an analysis of the results of transfusion of such blood. Just as some questions which arise as to the limitations of bank blood are answered by inquiry into the changes which occur in various components of blood when preserved, other, equally important questions, such as the effect of age of blood on the incidence and type of transfusion reactions, can be answered only by accurate recording of the results obtained from a long series of transfusions of bank blood. It is from this standpoint primarily that a statistical analysis of 3,077 consecutive transfusions of bank blood at the Cincinnati General Hospital becomes of interest. Numerous collateral points of interest which pertain to the practical operation of the service are also revealed by this study. These are of value to any one planning a similar organization and are commented on as they are presented.

A detailed description of the administration, headquarters and equipment and method of operation of the blood transfusion service, presented earlier, foretells the method by which the data were accumulated. The statistics presented were obtained from accurate records compiled at the time of transaction, from follow-up calls and from careful laboratory and case analyses when indicated.

DATA

TABLE 1.—*Donors to Blood Bank (Jan. 1, 1939, to Feb. 23, 1940)*

Group	White (64.2%)		Negro (35.8%)		Both Races	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
AB	52	2.3	47	3.8	99	2.9
A	925	41.3	368	29.5	1,293	37.1
B	184	8.2	262	21.0	446	12.8
O	1,079	48.2	570	45.7	1,649	47.2
Total	2,240	100.0	1,247	100.0	3,487	100.0

From the Department of Surgery of the University of Cincinnati College of Medicine and the Cincinnati General Hospital.

COMMENT

Of 3,487 donors who gave blood to the bank in the period from Jan. 1, 1939, to Feb. 23, 1940, 64.2 per cent were white and 35.8 per cent were Negroes. The percentage of occurrence of each of the four blood groups among the donors is given. A higher incidence of groups AB and B and a lower incidence of group A were present among the Negro donors. This concurs with numerous anthropologic observations.[1]

TABLE 2.—*Incidence of Syphilis Among Donors*

	Number of Donors	Positive Kahn Reactions	
		Number	Per Cent
White	2,240	58	2.6
Negro	1,247	203	16.2
Total	3,487	261	7.5

COMMENT

All prospective donors giving a history of syphilis were rejected. Despite this practice, 7.5 per cent of the blood drawn could not be used for transfusion because of positive Kahn reactions. In the white donor series the incidence of positive reactions for syphilis was 2.6 per cent as compared with 16.2 per cent for the group of Negro donors.

The loss due to syphilis could be eliminated by making tests before drawing blood for transfusion. However, if these tests were made through regularly scheduled morning laboratory procedure, prospective donors would have to return on the following day. Experience before the advent of the blood bank shows that many fail to return. If rapid tests were made preliminary to each drawing, additional expense for technical assistance would be necessary.

TABLE 3.—*Number of Donors Used and Transfusions Given*

	Number	Per Cent
Donors	3,487	100.0
Transfusions	3,077	88.2
Units discarded	410	11.8
Owing to		
Syphilis	261	7.53
Age	95	2.72
Clotting	51	1.46
Breakage	3	0.09
	410	11.80

1. Wiener, A. S.: Blood Groups and Blood Transfusion, Springfield, Ill., Charles C. Thomas, Publisher, 1939.

COMMENT

Of the 3,487 units of blood drawn, 3,077, or 88.2 per cent, were given in transfusion. Four hundred and ten units and half-units were discarded; in all but 149 instances this was due to positive reactions for syphilis. Ninety-five units and half-units were lost because the time limit of twenty-one days had expired before they could be used. Most of this loss occurred during the early operation of the bank and was the result of accumulation of half-units not desired and of the rarer groups AB and B when encountered in families of donors. Anticipation of overstocking of this kind improved as operation of the bank progressed, and this loss was reduced in the later months of operation by determining the group when necessary before drawing blood. The waste of the remaining 54 units resulted from clotting because of insufficient agitation or difficulty with veins during the drawing and from breakage. There was no loss due to bacterial contamination. Much of the blood discarded became useful in various experimental laboratories.[2]

TABLE 4.—*Transfusions Given According to Hospital Service*

Service	Number	Per Cent
Surgery	1,265	41.11
Medicine	589	19.14
Gynecology	435	14.13
Pediatrics	227	7.37
Urology	150	4.87
Obstetrics	131	4.25
Contagious diseases	94	3.05
Dermatology	86	2.79
Otolaryngology	62	2.01
Orthopedics	24	0.78
Ophthalmology	7	0.22
Psychiatry	7	0.22
Total	3,077	100.00

COMMENT

The amount of blood given in each hospital service in relation to the total is about what would be expected in a general hospital. Knowledge of the exact relation becomes of value in actual operation in prorating bank debits over the various services. Actually the number of transfusions given in the pediatric service is much higher than is stated. The figure expressed represents the number of units or half-units issued from the bank and does not take into account the fractional transfusion of some units, a practice most common in the pediatric service.[3]

2. Schiff, L.; Stevens, R. J.; Goodman, S.; Garber, E., and Lublin, A.: Observations on the Oral Administration of Citrated Blood in Man, Am. J. Digest. Dis. **6**:597, 1939.

3. In this report the number of transfusions corresponds to the number of units and half-units of blood issued from the blood bank. Actually the number of transfusions was larger, because some of these were divided and given as multiple transfusions.

TABLE 5.—*Transfusions from Blood Bank (Jan. 1, 1939, to Feb. 23, 1940)*

Group	White (68.9%)		Negro (31.1%)		Both Races	
	Number	Per Cent	Number	Per Cent	Number	Per Cent
AB	41	2.0	23	2.4	64	2.1
A	915	43.1	274	28.7	1,189	38.6
B	162	7.6	177	18.5	339	11.0
O	1,003	47.3	482	50.4	1,485	48.3
Total	2,121	100.0	956	100.0	3,077	100.0

COMMENT

Three thousand and seventy-seven units and half-units of blood were issued from the bank and given in transfusion. The distribution of these units and half-units according to race and to the four blood groups is recorded in table 5.

TABLE 6.—*Transfusions of Unlike Groups*

Groups	Number	Per Cent
O — B	31	26.7
O — A	50	43.1
O — AB	1	0.9
A — AB	18	15.5
B — AB	16	13.8
Total	116	100.0
Total transfusions of unlike groups	116	3.8
Total transfusions of like groups	2,961	96.2
Total transfusions in series	3,077	100.0

COMMENT

Of the 3,077 transfusions given, 2,961, or 96.2 per cent, represented transfusions of like groups. In only 3.8 per cent of the cases was the bank unable to supply the group requested. The universal donor and universal recipient principle was applied in each of the 116 cases in which it was necessary only after a preliminary direct match, the Coca compatibility test being used.[4] In the absence of group AB blood, group A or group B blood was always selected in preference to group O, because only one incompatible agglutinin-agglutinogen complex is dealt with in the dilution principle.

TABLE 7.—*Incidence of Transfusion Reactions*

	Number	Per Cent
Transfusions	3,077	100.0
Reactions		
Hemolytic	2 *	0.06
Febrile	125	4.06
Urticarial	56	1.82
Total	183	5.94

* One questionable.

4. Hoxworth, P., and Ames, A.: Blood Grouping and Compatibility, J. A. M. A. **108**:1234 (April 10) 1937.

TABLE 8.—*Types of Transfusion Reactions*

	Number	Per Cent
Hemolytic	2 *	1.1
Febrile with chill	95	
Febrile	30	68.3
Mild urticarial	53	
Severe urticarial	3	30.6
Total	183	100.0

* One questionable.

COMMENT

Any report on the incidence of unfavorable transfusion reactions must necessarily be affected by the author's definition of a transfusion reaction. Subjective complaints not accompanied with any related objective, clinical or laboratory abnormalities during or after the transfusion have been disregarded in this presentation. All reactions occurring in this series are classified as hemolytic, febrile or urticarial. Untoward reactions occurred after 5.94 per cent of the 3,077 transfusions given. Of the two hemolytic transfusion reactions reported, one was the result of a laboratory error in which group A blood was given to a person whose blood was group O, and the other, which is not well established, resulted from the transfusion of group A blood to a person whose blood was group A. The following reports present the clinical and laboratory data in each instance.

REPORT OF CASES

CASE 1.—A white man aged 55 years, with pyloric obstruction due to a duodenal ulcer, received a preoperative blood transfusion on Aug. 1, 1939. Blood of group A was given to the patient, whose blood group was later determined as O. The laboratory technician had, by mistake, performed the grouping and compatibility tests on a specimen of group A blood which had become confused with the specimen from the patient. Approximately 75 cc. of citrated blood had been given when the patient suddenly complained of precordial pain and a sensation of tingling in both lower extremities. The transfusion was stopped at this point. Pallor and dyspnea were noted; the radial pulse could not be felt, and the systolic pressure fell to zero. There were vomiting and diarrhea. Treatment for shock was instituted, and the blood pressure rapidly rose to 150 systolic and 110 diastolic. A severe shaking chill occurred twenty minutes later, followed by cyanosis. The patient was placed in an oxygen tent, and his general condition was good from that time on. Five hours after the transfusion he complained of cramps in the gastrocnemius muscles. Twelve hours after the transfusion he voided urine for the first time; 150 cc. of dark brown, smoky urine was passed. Examination of the urine revealed a 4 plus benzidine reaction, a few granular casts, a 3 plus reaction for albumin, a specific gravity of 1.015 and a p_H of 6. The urinary abnormalities gradually disappeared over a period of three days. On the day following the transfusion the urea nitrogen content of the blood was 40 mg. per hundred cubic centimeters. One day later, the value was 26 mg. per hundred cubic centimeters and the carbon dioxide–combining power was 49 volumes per cent. On the third day the value for urea nitrogen was 25 mg. per hundred cubic centimeters, and the carbon dioxide–combining power was 59 volumes per cent. The blood chemistry was normal on the fourth day. Two days later, on August 7, a subtotal gastric resection was performed, and the postoperative course was uneventful.

CASE 2.—A white woman aged 34 was admitted to the medical service on Jan. 5, 1940. A diagnosis of chronic myelogenous leukemia had been established in July 1938. On admission to the hospital the patient was complaining of pain in the chest and in the left upper abdominal quadrant, severe coughing and gross hemoptysis. Examination revealed rales over both lung fields and a pleural friction rub over the base of the left lung. The spleen was palpable and tender. A clinical impression of pulmonary and splenic infarction was made. During the next two days the general course was progressively downhill, with a temperature of 104 to 105 F., a pulse rate ranging from 140 to 150 and a respiratory rate varying from 30 to 40, accompanied with cyanosis. The red blood cell count fell from 3,700,000 per cubic millimeter on admission to 2,510,000 on the fourth day in the hospital. The patient appeared moribund on the fifth day, when a transfusion of 300 cc. of citrated blood was given. Three and one-half hours later she complained of severe generalized abdominal pain and progressed almost immediately into a state of profound shock. A specimen of urine voided just before the onset of abdominal pain was recorded as dark red and gave a strongly positive reaction to benzidine. Death followed fifteen minutes after the occurrence of abdominal pain.

Permission for autopsy was not obtained, and unfortunately, the transfusion service did not learn of the death until twenty-four hours later, at which time the body had been embalmed. For these reasons laboratory and tissue studies sufficient to prove a diagnosis of hemolytic transfusion reaction were not possible.

COMMENT

In case 2, the blood groups of the donor and the patient prior to transfusion were determined as A. There was no evidence of incompatibility on the direct match test. Reexamination of the specimens of blood obtained before transfusion revealed that the blood of the patient belonged to subgroup A_2 and that of the donor to subgroup A_1. The specimens were then sent to Alexander Wiener, serologist and bacteriologist in the office of the chief medical examiner of New York city. Results of his examination also showed the blood of the patient to belong to subgroup A_2 and that of the donor to subgroup A_1. Wiener also found the blood of the patient to be Rh + and that of the donor to be Rh — and stated that this agglutinogen therefore could not have played any role in the reaction. He concurred with the opinion that a hemolytic transfusion reaction was not proved and stated that if this were a transfusion reaction it would have to be considered an unexplained one not avoidable by any of the technics available at present. This case is reported because the death was the only one in the entire series which might be attributed to the transfusion of blood.

Because of the known susceptibility of patients suffering from leukemia to severe transfusion reactions, some authorities on blood transfusion consider leukemia a contraindication to blood transfusion.[1]

In reporting this series of transfusions the following case is also of interest.

CASE 3.—A white man aged 32 years received a transfusion one hour after appendectomy for acute appendicitis with perforation. The patient's blood was of group A, and he had received 300 cc. of group B blood issued from the bank by mistake before the technician had realized the error. No signs of immediate or delayed reaction, subjective or objective, developed, despite close watching of the patient. All post-transfusion urinary specimens were examined for six days; there was no evidence of hemoglobinuria. The patient was discharged from the hospital on the twentieth postoperative day and was seen one month later in the follow-up clinic. No ill effects resulted from the transfusion of incompatible blood. Recheck of both the pretransfusion and the post-transfusion specimens of blood showed that of the patient to be group A and that of the donor to be group B. The incompatibility on direct match was evident in both specimens.

Febrile reactions followed 125 transfusions in this series, a percentage of 4.06. In 95 cases the rise in temperature was preceded by a chill. There were no deaths of which these reactions were considered a contributory cause. In 53 cases urticarial reactions marked only by the appearance of wheals followed close on transfusion. In 3 cases widespread urticaria was preceded by pallor, sweating, a marked increase in pulse rate and a fall in blood pressure. Each of the patients responded readily to supportive measures instituted for anaphylactic shock.

The incidence of urticarial reactions might be reduced if blood were drawn from donors in a fasting state. The difficulty and inconvenience of obtaining such donors make this plan impracticable, particularly in view of the mildness and infrequency of urticarial reactions.

TABLE 9.—*Febrile Reactions in Relation to Groups Transfused*

Groups	No. of Cases	Reactions	Febrile	Per Cent
AB — AB	64	3	2	3.1
A — A *	1,171	78	56	4.7
B — B	323	23	16	4.9
O — O	1,403	73	47	3.3
O — AB	1	0	0	0
B — AB	16	2	2	12.5
O — A	49	1	1	2.0
O — B	31	1	1	3.2
A — AB	18	0	0	0

* A — A series corrected for patient No. 78095
A — A transfusions 1,171 — 60 = 1,111
A — A febrile reactions 56 — 11 = 45
Corrected determination 45/1,111 = 4.0 per cent,

TABLE 10.—*Data on a Patient (Blood Group A) with Chronic Lymphatic Leukemia*

	Number	Per Cent
Transfusions given	61	
Transfusions of group A blood	60	
Transfusions of group O blood	1	
Febrile reactions	12 *	19.7
Urticarial reactions	6	9.8
Total reactions	18	29.5

* One reaction was O — A.

COMMENT

The causes of chills and fever which follow intravenous administration of solutions, including blood, and methods for reducing the incidence of these reactions have been a subject of much interest in many hospitals. The adoption of rigid routines in the preparation of solutions and cleansing of glassware and tubing with which the solutions come in contact have reduced the incidence of untoward reactions. Despite careful attention to these factors, the incidence of chills and fever in most reported series of blood transfusions varies from 5 per cent to 20 per cent. In addition to extrinsic factors it is probably true that the condition of the patient plays a role in causation of these reactions. It is a matter of common observation that patients in severe septic states and with leukemia, for example, are much more subject to post-transfusion chills and fever.

Recently some writers[5] have contended that the subgroups of A and AB, namely, A_1, A_2, A_1B and A_2B, when mixed in transfusions, may be responsible for post-transfusion chills and fever. For this reason the transfusions in this series were analyzed from the standpoint of febrile reactions in relation to blood groups transfused. The incidence of febrile reactions was 4.7 per cent between members of group A, 4.9 per cent between members of group B and 3.3 per cent between members of group O. While the percentage of reactions occurring among members of group A was no higher than that observed among members of group B, both of these series revealed a higher percentage than occurred among members of group O. It may be that the number of transfusions given members of group B is not sufficiently large to permit any value to be attached to a percentage analysis. Considering this, the incidence of reactions among 1,171 transfusions of group A blood to group A patients (4.7 per cent), as compared to those in which group O was concerned (3.3 per cent), is considerably higher. However, in the group A series, 1 patient received sixty-one transfusions for anemia secondary to chronic lymphatic leukemia. Febrile reactions followed twelve of the sixty-one transfusions, and urticarial reactions followed six, making a total of eighteen. The total incidence of reactions was 29.5 per cent and that of febrile reactions 19.7 per cent. One of the febrile reactions followed a transfusion of group O blood, leaving eleven febrile reactions in sixty transfusions of group A blood. A truer analysis of the group A reactions results if the series is corrected by eliminating the transfusions and reactions of this patient, since in the group O series no patient particularly susceptible to reactions received a comparable number of trans-

5. Davidsohn, I.: A Method for Recognition of Blood Subgroups A_1 and A_2, J. A. M. A. **112**:713 (Feb. 25) 1939. Blinow, N. I.: Subgroups A_1 and A_2 and Their Practical Significance, Sovet. khir. **7**:335, 1934.

fusions. The corrected reaction rate in the group A series is 4 per cent, which is very close to the rate of 3.3 per cent in the group O series, and the difference is not significant, being well within the limits of statistical error when the number of cases reported is considered.

TABLE 11.—*Relation of Reactions to Age of Blood Transfused*

Age of Blood in Days	Number of Transfusions	Febrile		Urticarial	
		Number	Per Cent	Number	Per Cent
1	468	21	4.5	19	4.1
2	540	25	4.6	9	1.1
3	386	13	3.4	5	1.3
4	286	10	3.5	2	0.7
5	248	13	5.2	5	2.0
6	230	10	4.3	4	1.7
7	182	6	3.3	2	1.1
8	140	5	3.6	3	2.1
9	110	2	1.8	1	0.9
10	93	4	4.3	1	1.1
11	99	4	4.4	3	3.0
12	64	2	3.1	0	0
13	55	2	3.6	1	1.8
14	56	2	3.6	1	1.8
15	29	1	3.5	0	0
16	20	2	10.0	0	0
17	16	2	12.5	0	0
18	7	1	14.3	0	0
19	5	0	0	0	0
20	2	0	0	0	0
21	1	0	0	0	0
Total	3,077	125		56	

COMMENT

Whether the incidence of reaction increases as bank blood ages is another subject of much interest. Because of this the transfusions given in this series are analyzed from the standpoint of reactions in relation to the age of the blood given. This analysis will become of real value as more statistics are accumulated. At present the figures indicate that the aging of blood does not increase the incidence of reactions.

Another point of interest shown in this analysis is that in practical operation the great majority of bank blood units given are under 7 days of age. Thus the age limitations of bank blood, which have been fairly well established, can be met without difficulty.

SUMMARY AND CONCLUSIONS

An analysis of the experience gained and statistics derived from 3,077 transfusions of bank blood at the Cincinnati General Hospital is presented. This was made in order to study the effects of transfusion of preserved blood and also to provide information helpful in the actual operation of a blood bank.

The results may be summarized as follows:

1. Blood of the same group as that of the patient is available without delay in 96 per cent of the cases.

2. The incidence of untoward transfusion reactions compares favorably with that in reported series of transfusions of fresh blood.

3. Aging of blood does not increase the incidence of febrile reactions.

4. There is no significant increase in untoward reactions resulting from transfusion of group A blood as compared with transfusion of blood of the other groups.

5. The causes of loss of bank blood are, in order, positive reactions for syphilis, expirations of the time limit and clotting. Methods for minimizing these losses are suggested.

6. In the 3,077 transfusions of blood given, only 1 death occurred which might be attributed to the transfusion.

RESECTION OF THE COLON BY INTUSSUSCEPTION

A ONE STAGE INTERIORIZATION PROCEDURE RESULTING IN AN END TO END ANASTOMOSIS

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More than two hundred and seventy-five technical procedures [1] have been devised to diminish the amount of contamination of the peritoneal cavity incidental to resection of portions of the large bowel. The fact that no method has yet proved entirely satisfactory has led to attempts to reduce the risk of infection by measures directed toward increasing the resistance of the patient. These attempts have consisted for the most part of more careful preoperative preparation of the patient, use of intraperitoneal injections designed to increase local immunity and more widespread use of multiple stage operations.

In general, the technical procedures for extirpation of a portion of the colon with subsequent reestablishment of intestinal continuity may be divided into two groups. In one group, the peritoneum and the bowel are opened at the same time, and the various technics are directed toward securing the least possible amount of soiling, either by appropriate isolation of the open bowel with towels and sponges or by keeping the bowel temporarily closed by various methods until after the anastomosis has been completed.

The object of the technics employed in the second group is to have both the resection and the subsequent restoration of continuity of the bowel performed at a time when the peritoneum is not open. This is accomplished by extra-abdominal exteriorization of the offending lesion, with delayed resection and subsequent anastomosis by gradually crushing the spur between the two limbs of the fecal fistula.[2]

The fundamental difference between these two groups of procedures lies in the fact that with immediate resection and anastomosis the spread

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1. Poth, E. J.: A Clean Intestinal Anastomosis, Arch. Surg. **28**:1087 (June) 1934.

2. Bloch, O.: On Extra-Abdominal Treatment of Intestinal Cancer, Nord. med. ark. **24**:1, 1892. Paul, F. T.: Colectomy, Brit. M. J. **1**:1136, 1895. Von Mikulicz, J.: Small Contributions to the Surgery of the Intestinal Tract, Boston M. & S. J. **148**:608, 1903.

of bacteria from the lumen of the intestine starts at the same time that fibrinous agglutination of the opposed serous surfaces begins, so that occasionally the establishment of an effective fibrinous barrier may be delayed and postoperative intraperitoneal leakage of intestinal contents may ensue. In the exteriorization type of procedure, this fibrinous barrier is established before the spread of bacteria begins and therefore the danger of intraperitoneal contamination is considerably diminished.

Because of this fundamental difference, the exteriorization procedures possess certain physiologic advantages which could never be attained by the methods involving immediate resection and anastomosis. Unfortunately, they also have numerous well known disadvantages, such as inability to resect widely the mesentery and the presence of a temporary artificial anus, which tend to restrict their general use.

In considering both the advantages and disadvantages of these two methods, one realizes that the ideal procedure would be a combination of the two, that is, an intraintestinal interiorization of the lesion, with delayed necrosis of the interiorized portion resulting in an end to end anastomosis.

This ideal (resection with anastomosis) is occasionally accomplished by nature as the result of spontaneous intussusception of a lesion of the colon, with subsequent slough of the intussusceptum. Unfortunately, such a favorable result is not often observed, because of the disastrous effects of strangulation and intestinal obstruction. For this reason, operative reduction of the intussusception is usually attempted for conditions which do not respond to conservative therapy.

It is interesting to note the frequency with which this spontaneous sloughing of an intussusceptum occurred before the advent of modern abdominal surgery. In 1874, Leichtenstern [3] reported a series of 593 cases of intussusception, in 29 per cent of which there were spontaneous necrosis and elimination of the intussusceptum. Of the 170 cases of "spontaneous elimination," 149 were followed over a sufficient period to determine that recovery occurred in 59 per cent.

In spite of the rather obvious dangers of spontaneous intussusception, limited clinical application of nature's method of resection has previously been attempted in a virtually unmodified form. Thus, in 1895 Guinard [4] reported 2 cases in which he had invaginated segments of the small intestine. In the first of these, 9 cm. of gangrenous bowel was invaginated, and in the second, two gangrenous rings of intestine which had been located at the neck of the sac of a strangulated hernia were invaginated. The patients in both cases recovered. In 1908,

3. Leichtenstern, O.: Ueber Darm-Invagination: III, Vrtljschr. f. d. prakt. Heilk. **121**:17, 1874.

4. Guinard, A.: Traitement des hernies gangrenées par l'invagination totale ou partielle, Assoc. franç. de chir., Proc.-verb. **9**:455, 1895.

Summers [5] described 2 cases of annular gangrene of the small intestine treated by invagination, and in 1927 he referred to 5 additional cases in which this method was used. There were 2 deaths in this series of 7 cases. He stated that he restricted his use of the method to cases in which the invaginated portion would not exceed 5 cm. in length, because of a fear of intestinal obstruction and of difficulty in producing the invagination. In both Guinard's and Summers' cases the arterial blood supply of the bowel which was invaginated was already so affected that further changes resulting from strangulation could not occur. This probably accounts for their success.

It would seem that successful development of this natural intussuscepting type of intestinal resection would depend on (1) avoidance of strangulation; (2) prevention of intestinal obstruction; (3) development of a method by which an intussusception might be readily produced, and (4) utilization of some method assuring delayed amputation of the intussusception.

The dangers of strangulation may be greatly diminished by removal of the mesocolon from the bowel which is to be invaginated. Intestinal obstruction may be avoided and invagination of the bowel easily produced by the appropriate use of a rubber tube, the technic of which is described subsequently. Although spontaneous necrosis would result in amputation of that portion of the bowel which was deprived of its blood supply through division of the mesentery, delayed amputation of the intussusceptum at points proximal to this level of viability may be obtained by occlusion of the intramural blood supply with an elastic ligature.

TECHNIC

The accompanying illustrations are designed to show the important steps of this operation as it is performed on the dog. The ileocecal region was chosen because it would seem to offer those difficulties which would probably be encountered in man. Thus, it is the region of the colon most distant from the anus; the dog's appendix affords a considerable bulk for invagination, and it could be shown that in this animal, at least, a tube can be passed through the ileocecal valve for a considerable distance into the ileum.

The following paragraphs are devoted to a description of the technical details of this procedure. For the sake of simplicity, these details are presented in sections corresponding roughly to the steps shown in the illustrations.

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5. Summers, J. E.: Invagination of Limited Annular Gangrene of the Small Bowel Versus Resection, J. A. M. A. **51**:472 (Aug. 8) 1908; The Treatment of Annular Gangrene of the Small Bowel by Invagination Versus Resection, Surg., Gynec. & Obst. **44**:374, 1927.

1. The immediate preparation for operation consists of thorough cleansing of the bowel distal to the segment to be resected and construction of the tube which is to be used both for production of the intussusception and relief of postoperative distention of the bowel proximal to the intussusception.

The rubber tube which was used in the experimental evolution of this technic was the one most convenient at the time. It was made of ordinary hard red rubber suction tubing approximately 1 cm. in diameter. In its preparation two rather prominent rolls of adhesive tape, designed to hold the initial, "intussuscepting" ligature, are placed on the tube, far enough from its end to insure protrusion of the tube into the proximal portion of the bowel after completion of the intussusception. This distance is usually approximately two thirds of the expected length of the segment of bowel to be resected. Near the end of the tube are placed several smaller rolls of adhesive tape to prevent slipping of the final necrotizing ligature when the intussusception is doubled over it. The latter rolls are an accessory rather than a necessity (fig. 1).

At operation the segment of bowel to be resected is mobilized, and its mesentery is removed. This preliminary resection of the mesentery not only eliminates subsequent strangulation, with its concomitant intestinal obstruction, but enables the operator to carry out the necessary manipulations of the bowel on a segment which has been both denervated and devascularized, thus eliminating this manipulation as a possible source of surgical shock. Clinically it might also be thought of as a prophylactic measure against possible metastasis of embolic tumor.

An assistant passes the tube by rectum until it is felt near the peritoneal reflection of the rectum by the operator. The latter then directs the end of the tube up the colon and assists it in its passage through the segment to be resected. When passage of the tube has been completed, the two larger rolls of adhesive tape should be so situated that the interval between them will be approximately 2 to 3 cm. proximal to the center of the loop to be resected. This adds sufficient length to the outer layer of the intussusceptum to permit doubling of the intussusception after the application of the final necrotizing ligature.

A ligature of umbilical tape is then placed about the bowel and tied so that it lies in the space between the two larger rolls of adhesive tape (fig. 1). Umbilical tape or similar relatively broad ligature material is used for this purpose because adequate friction can be obtained without tying the ligature tight enough to diminish the lumen of the tube.

2. After the bowel has been anchored to the tube, the portion of the segment distal to the ligature is grasped by the operator, and downward traction is applied to the anal end of the tubes by an assistant (fig. 2*A*). An intussusception is readily produced and increased to a point at which the base of the intussusception is approximately 1.5 to 2 cm. from the mesenteric borders. The reason for stopping the intussusception at this point is to leave sufficient viable bowel above the base of the intussusception for completion of the anastomosis.

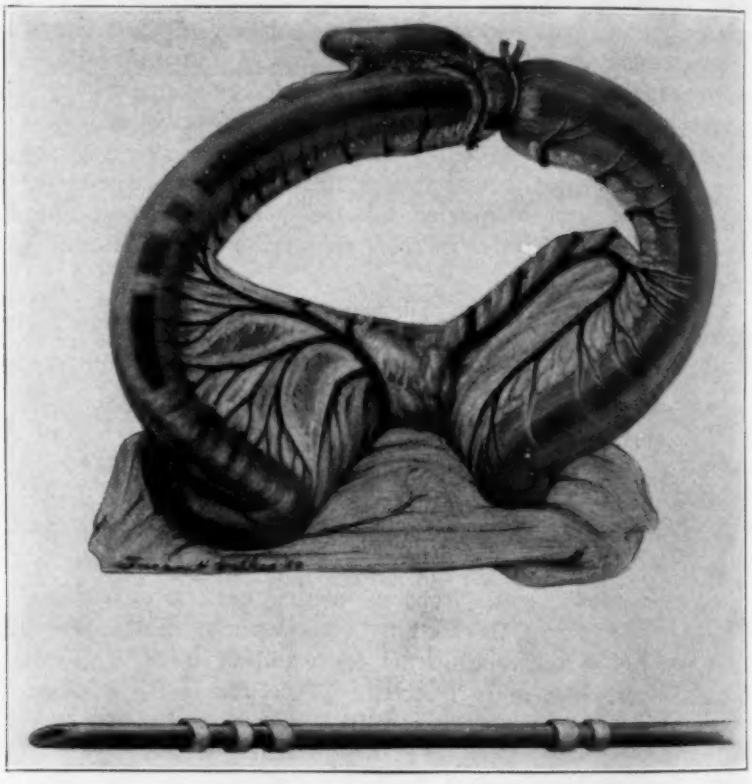

Fig. 1.—The mesentery of the segment to be resected has been removed. A rubber tube has been passed by rectum through this segment and a ligature tied about the bowel between two narrow rolls of adhesive tape on the indwelling tube. This ligature should be slightly proximal to the midportion of the segment to be resected. The rubber tube with the rolls of narrow adhesive tape in place is shown at the bottom of the picture.

3. Another ligature of umbilical tape is tied about the base of the intussusception to maintain it and subsequently serve as a fixed apex for the second intussusception. Care should be exercised in the placement of this ligature, so that the smallest possible lip of the intussus-

cipiens is proximal to it (fig. 2*B*). If the ligature should fall just distal to one of the smaller rolls of adhesive tape, it will help considerably in the next step (doubling the intussusception), for the small roll of adhesive tape will impinge on the ligature when downward traction is made. However, this is not essential for effective doubling of the intussusception.

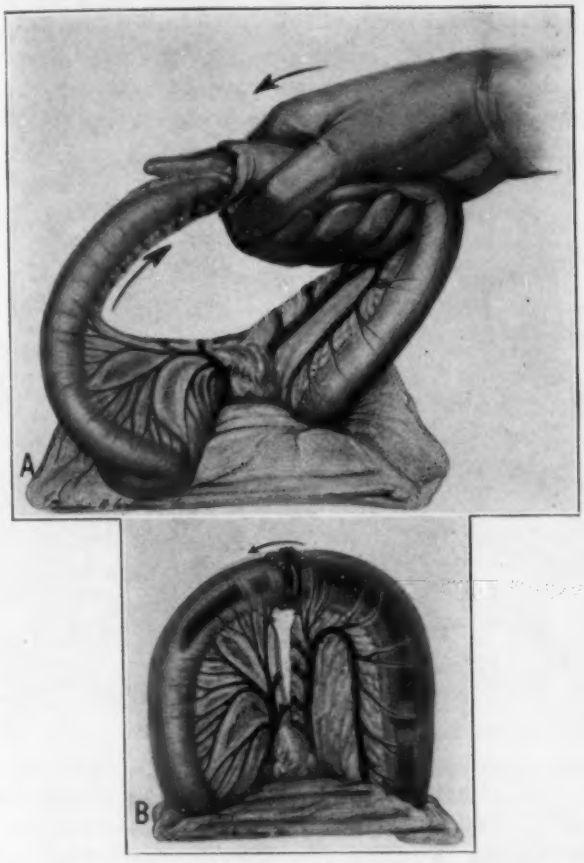

Fig. 2.—*A*, downward traction on the anal end of the indwelling tube by an assistant, together with countertraction on the intussuscipiens by the operator, readily produces an intussusception. *B*, the initial intussusception has been completed to within approximately 2 cm. of the mesenteric borders, and the necrotizing ligatures have been tied about its base. The arrow shows how the bowel is to be reintussuscepted over these ligatures.

Although it would appear at first that this ligature would be sufficient to produce necrosis of all the intussusceptum distal to it, experience has shown that it does not invariably do so. Therefore, a rubber

band is also tied snugly about the base of the intussusception. This effectively amputates the intussusceptum through all of its layers. Use of the rubber ligature alone is not advisable, because it has a tendency to roll when the intussusception is doubled over it and may thus considerably complicate a simple maneuver. I should also like to warn specifically against the application of crushing clamps to the base of the intussusception, for in several instances in which it was tried slight leakage of gas and fecal material from the crushed area was noted on removal of the clamps.

4. After the necrotizing ligatures have been placed, the bowel is grasped as before, and further traction is applied to the rectal tube.

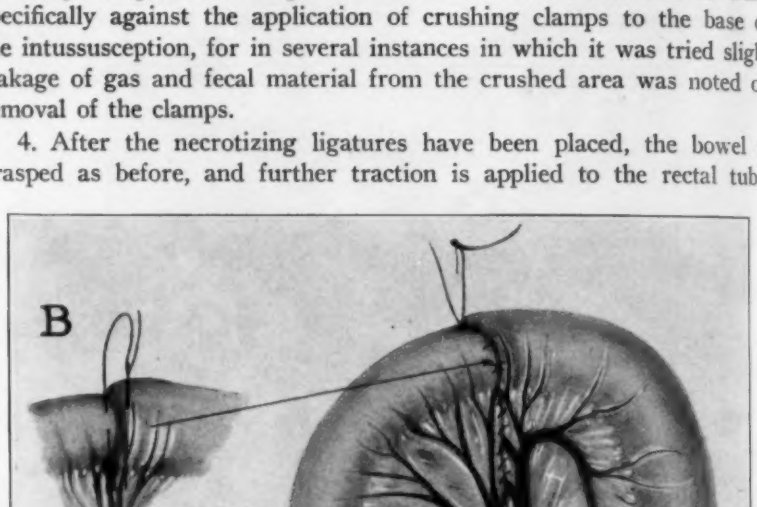

Fig. 3.—The second intussusception has been produced and interrupted submucosal sutures placed between the bowel above and the intussuscipiens below. One of these sutures is left long so that it may later be sewed to the parietal peritoneum to forestall any further intussusception. A second row of anastomotic sutures is placed about the circumference of the bowel (not shown). The defect in the mesentery has been repaired. *A*, cross section of the anastomosis, showing nonapposition of the mesenteric borders. *B*, simple right angle suture used to secure serosal approximation in this type of anastomosis.

This produces another, very short intussusception over the two ligatures at the base of the first intussusception; that is, a double intussusception is produced with the apex of the second, short, viable intussusceptum, being marked by the ligatures which are destined to produce necrosis of the first, relatively long intussusceptum. Successful completion of

the anastomosis is dependent on securing accurate approximation of the serosal surfaces of the layers of this short intussusceptum.

MacFee[6] and others have drawn attention to the importance of carefully removing the fat from the surfaces to be approximated as well as carefully ligating all vessels in the line of anastomosis. In so doing one also removes a relatively large portion of the serosa, the fat lying for the most part between the leaves of the mesentery at the point where they separate to envelop the bowel. This removal of fat and serosa from the wall of the bowel results in an increase in the normally present "bare" area at the mesenteric border, and, because of the loss of the specific adhesive characteristic of peritoneum, approximation of two such "bare" areas would theoretically be expected to increase the danger of postoperative leakage. In this connection, Mayo[7] stated: "I have watched surgeons use great care to keep the mesenteric attachments adjusted exactly to each other in making an end to end anastomosis of the intestine. This leaves two fat areas, without peritoneum, joined to each other. If the bowel is rotated a quarter of an inch, an area with perfect peritoneal protection is joined to an area that has no such protection, union is immediate, and peristalsis is not interfered with in any way." This principle of contrarotation of the mesenteric borders seems to eliminate the "bare" areas as possible regions of ineffective fibrinous agglutination (fig. 3*A*).

The problem of approximating sutures in this intussuscepting type of anastomosis is somewhat different from that encountered in the conventional end to end anastomosis, for whereas in the latter the prime purpose is the abutment of two surfaces at right angles to the long axis of the bowel, in this type the desired effect is an approximation of two serosal surfaces which lie in a plane parallel to the long axis of the bowel. Thus, for example, although the Halsted square mattress suture is ideally suited for abutment, it is not so satisfactory for approximation in parallel.

In securing the latter type of approximation, I have found the simple right angle suture to be extremely easy to place and entirely satisfactory (fig. 3*B*). In its application, care is taken to secure a bit of the submucosa, and penetration into the lumen is guarded against.[8] One of the first row of interrupted sutures is left long so that later it may be attached to the parietal peritoneum to forestall any further intus-

6. MacFee, W. F.: Resection with Aseptic End-to-End Anastomosis for Carcinoma of the Colon, Ann. Surg. **106**:701, 1937.

7. Mayo, C. H.: Wrinkles and Recipes in Intestinal Surgery, Ann. Surg. **98**: 830, 1933.

8. Halsted, W. S.: Circular Suture of the Intestine: An Experimental Study, Am. J. M. Sc. **94**:436, 1887; Surgical Papers, Baltimore, Johns Hopkins Press, 1924, vol. 1, p. 185.

susception. For the second row of anastomotic sutures I have used the Cushing continuous right angle suture around the entire circumference of the bowel. Martzloff, Moore and Gardner,[9] in a large series of experimental intestinal anastomoses, have reported that the incidence of postoperative leakage was considerably less with silk than with other types of suture material. Therefore, only silk has been used in this series of resections.

After completion of the anastomosis, the operation is finished in the usual manner. The mesenteric borders are approximated; an

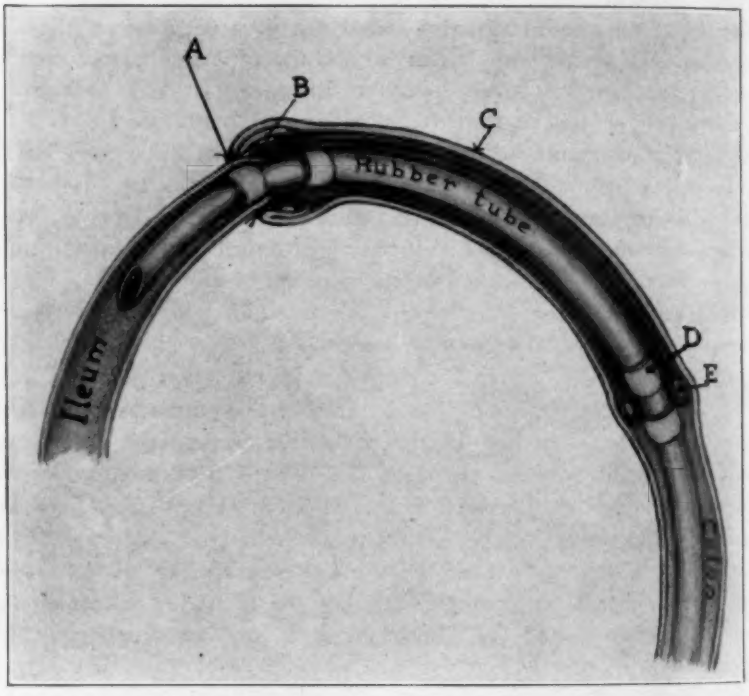

Fig. 4.—Diagram of a longitudinal section through the completed anastomosis. *A*, serosal approximating sutures; *B*, necrotizing ligatures which will produce necrosis of the shadowed intussusceptum (*B* to *E*); *C*, the intussuscipiens; *D*, rolls of adhesive tape on the indwelling rubber tube, which serve to hold the initial ligature; *E*, initial, or "intussuscepting," ligature.

opening is made in the omentum, and the uncut suture from the first row of anastomotic sutures is pulled through. This is then sewed to the parietal peritoneum, and the anastomosis is protected with omentum.

9. Martzloff, K. H.; Moore, P. H., and Gardner, J.: Aseptic End-to-End Intestinal Anastomosis: A Report of One Hundred and Ninety-Seven Experimental Anastomoses in Dogs, West. J. Surg. **47**:611, 1939.

The abdomen is closed, and the excess of rubber tubing which protrudes from the anus is removed. In dogs it has not been found necessary to fix the tube to the anal margin; it is left free and allowed to pass when the necrotizing ligature at the base of the initial intussusception cuts through.

EXPERIMENTAL RESULTS

This technic for resection of the bowel has been employed on 16 dogs. There were no early postoperative deaths, and convalescence

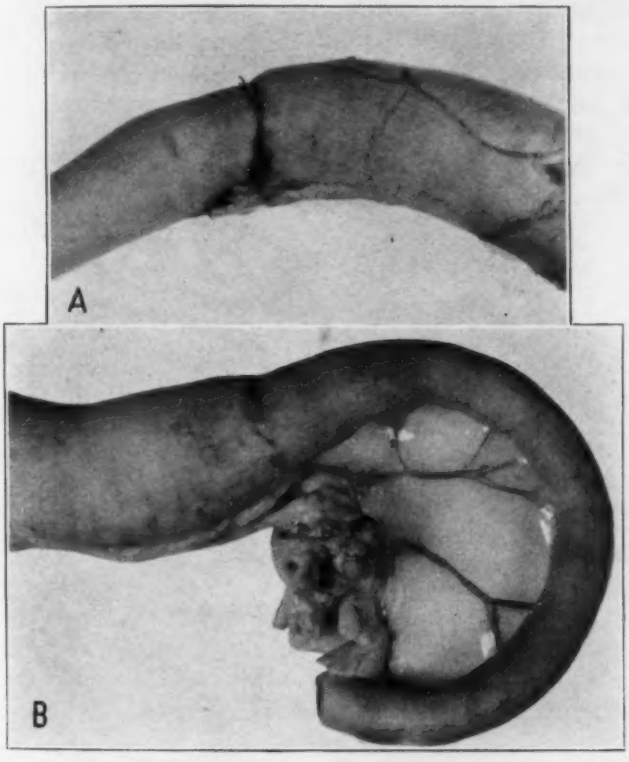

Fig. 5.—*A*, photograph of a specimen removed eight days after operation. *B*, photograph of a specimen removed thirty-three days after operation.

was uneventful in every instance. One dog died twenty days after the operation, of distemper, and another, rather old dog died forty-six days after operation, from an undiscovered cause. The peritoneal cavities in both of these dogs were free from infection; the anastomoses were in good condition, and there was no evidence of intestinal obstruction. The other dogs were killed for specimens at varying intervals after operation. In none was there any evidence of peritoneal inflammation or obstruction, but in most there was an omental adhesion about the

suture which had been sewn to the parietal peritoneum. A few of these specimens are shown in the accompanying illustrations (figs. 5, 6 and 7).

Eleven operations were performed in which the resected area included the ileocecal region and five in which the resected area was limited to different segments of the descending colon (there is no sigmoid flexure in the dog). Thus it was possible to vary the amount of bowel resected and the location of the anastomosis over a very wide range. The amount resected varied from resections of the colon and the terminal portion of the ileum in which the segment was between 3 and 4 feet (0.9 to 1.2 M.) in length to very limited resections of only a few centimeters. The location of the anastomosis varied from just distal to the ileocecal region to beneath the peritoneal reflection of the rectum.

After recovery from the intravenous pentobarbital sodium anesthesia, the dogs were allowed to take food or water as they desired.

Fig. 6.—Photograph of a specimen removed twenty days after resection of approximately 10 cm. of descending colon. The distal portion of the colon has been folded back to show the stoma of the healed anastomosis.

There was a latent period of several hours during which there was little, if any, drainage from the indwelling rectal tube, and then drainage began, continuing until the tube was extruded.

Necrosis of the intussusceptum usually became apparent within twelve hours after operation. With resections in which the intussusceptum remained entirely within the bowel gradual autolysis took place, so that the dogs would often pass small quantities of thin black fluid around the rectal tube. With resections in which the apex of the intussusceptum protruded through the anus the exposed portion became increasingly dark, shrinking gradually until a typical dry gangrene resulted.

The indwelling rectal tube was usually retained for thirty-six to forty-eight hours, but in a few instances, in which the animals were restrained so that they did not have impulses to defecate, this period was considerably longer. Extrusion of the tube was usually accom-

panied by a bowel movement, the excreta consisting of the fluid accumulated from autolysis of the intussusceptum together with incompletely digested strips of necrotic bowel. On the extruded tube would be found the various ligatures that had been tied about the bowel at operation.

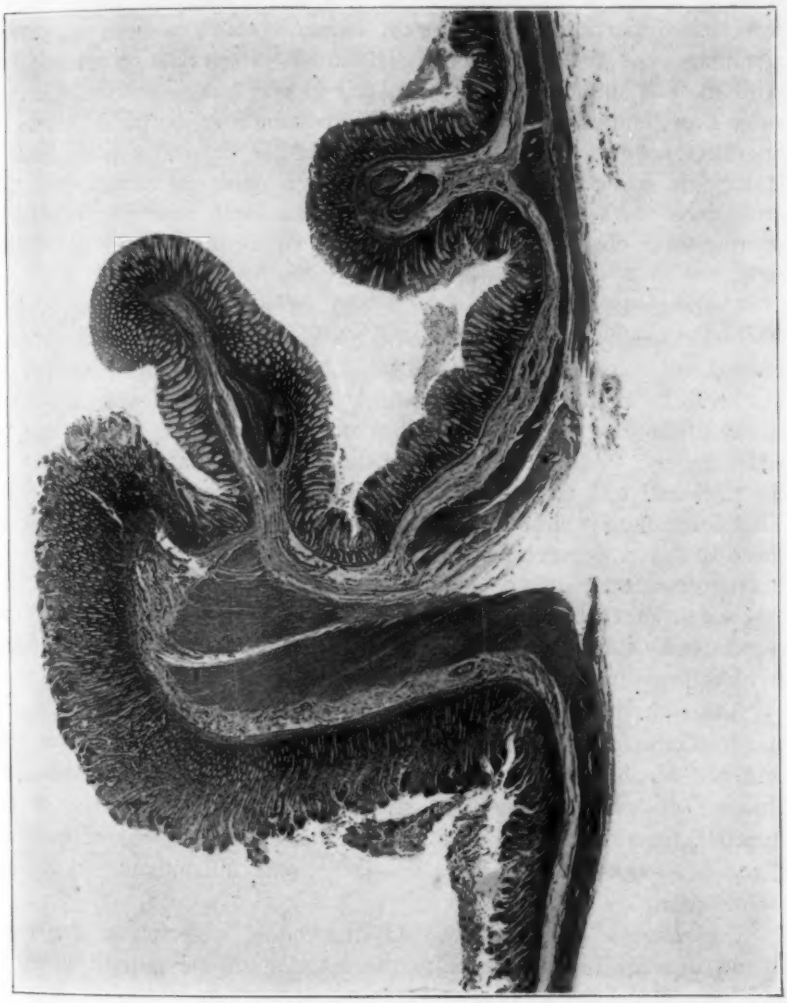

Fig. 7.—Photomicrograph showing the site of anastomosis in a specimen removed forty-nine days after operation. Hematoxylin and eosin; × 7.

After passage of the tube, normal intestinal habits were usually restored, but in a few instances, in which total colectomy had been performed, there was diarrhea which lasted for several weeks, with gradual return toward normal. In these animals the perianal region often became moderately excoriated.

COMMENT

A new method of resection and anastomosis of the colon based on intussusception has been evolved. Fundamentally the procedure consists of an intraintestinal interiorization of the segment to be resected into the lumen of the bowel distal to it and subsequent slough of the interiorized portion as a result of ischemia. It combines all of the advantages of the usual extra-abdominal exteriorization procedure,[1] with the obvious advantages of an end to end anastomosis and, at the same time, eliminates most of the disadvantages of both. Not only is operative soiling completely eliminated, but the danger of postoperative leakage is reduced to a minimum through delay in exposure of the anastomosis to fecal contamination. At the same time, the possibility of intestinal obstruction is avoided by use of an indwelling rubber tube.

Unfortunately, I have not yet had an opportunity to apply this method clinically, but I may predict to a certain extent what its indications and contraindications will be. Primarily, of course, its application will be limited to lesions which can be intussuscepted into the bowel distal to them. This implies not only that the lesion must be small enough to enter the bowel distal to it but that the character of the intestinal wall must be such that invagination may be accomplished. This immediately eliminates large, bulky lesions and those in which there is such a degree of intramural fibrosis as to preclude the folding-back process necessitated by the invagination. It is possible, however, that a fair percentage of medium to small tumors of the colon will be resectable by this procedure, as well as many lesions of prefibrotic ulcerative colitis, diverticulosis and multiple polyposis.

Although this type of resection of the colon is designed as a one stage interiorization operation, I should like to emphasize that the presence of obstruction or subacute perforation still necessitates preliminary diversion of the fecal stream proximal to the region to be resected, together with the lapse of sufficient time to insure minimal chances of contamination from the pericolonic inflammatory tissue on mobilization.

The range of application of this method of resection of the colon should increase in proportion to the increase in the number of early diagnoses of colonic lesions.

SUMMARY

An intussuscepting type of resection of the colon has been developed. This is a one stage intraintestinal interiorization procedure, which embodies the following steps: 1. The segment to be resected is mobilized and its mesentery removed. 2. A fairly stiff rubber tube is passed by rectum through this segment and anchored to the tube with a ligature. 3. Traction on the tube from below coupled with countertraction

on the intussuscipiens from above readily produces an intussusception. 4. This intussusception is increased to within 1.5 to 2 cm. of the mesenteric borders, and a necrotizing ligature is tied about its base. 5. With this ligature as its apex, another, very short intussusception is produced in the same manner as the first, and serosal approximating sutures are placed between the bowel above and the intussuscipiens below.

This technic for resection of the colon seems to preserve the asepsis of the usual extra-abdominal exteriorization procedure and at the same time presents the advantages of an end to end anastomosis, for in its use the lumen of the bowel is not opened, and exposure of the suture line to fecal contamination is deferred until the intussusceptum becomes necrotic prior to its spontaneous amputation.

This method for resection and anastomosis of the colon has been employed in 16 dogs. There were no early postoperative deaths, and convalescence was uneventful in every instance.

Dr. Alfred Blalock has given valuable suggestions and constructive advice during this study.

POSTOPERATIVE HYPOPROTHROMBINEMIA AND ANESTHESIA

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AND
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It is generally agreed that a reduction of the prothrombin content of the plasma frequently is seen during the postoperative period in patients with biliary fistula or obstructive jaundice. Such a reduction may occur even though preoperative correction of any prothrombin deficiency has been carried out through the medium of vitamin K and bile salt therapy. The hypoprothrombinemia seen in some of these patients may be so severe as to give rise to brisk hemorrhage during the postoperative period.[1]

The cause of the postoperative prothrombin reduction seen in many patients with biliary fistula or obstructive jaundice has been subjected to controversy. In theory the postoperative hypoprothrombinemia may be the result of three factors: (1) loss of prothrombin commensurate with the amount of blood lost; (2) damage to the liver attendant on surgical procedures and anesthesia, and finally (3) failure to reestablish the body's normal reserves of prothrombin or one of its precursors.

The point of view held by most workers has been that the anesthetic agents employed were capable of producing sufficient damage to the liver to account for any fall in prothrombin which might appear during the postoperative period.[2] At present there are no experimental data correlating hepatic damage and hypoprothrombinemia due to anesthesia to support this thesis except cases in which chloroform was the anesthetic agent.[3]

From the Department of Surgery of the University of Chicago.

This work has been aided by a grant from the Douglas Smith Foundation for Medical Research of the University of Chicago.

1. Stewart, J. D.: Prothrombin Deficiency and the Effects of Vitamin K in Obstructive Jaundice and Biliary Fistula, Ann. Surg. **109**:528, 1939.

2. Cullen, S. C.; Ziffern, S. E.; Gibson, R. B., and Smith, H. P.: Anesthesia and Liver Injury, with Special Reference to Plasma Prothrombin Levels, J. A. M. A. **115**:991 (Sept. 21) 1940.

3. Warren, R., and Rhoads, J. E.: The Hepatic Origin of the Plasma-Prothrombin Observations After Total Hepatectomy in the Dog, Am. J. M. Sc. **198**:193, 1939.

Lord [4] emphasized the factor of mechanical trauma to the liver associated with surgical procedures as a possible cause of the postoperative hypoprothrombinemia, and he demonstrated that such a prothrombin reduction can be experimentally produced in dogs by massaging the liver at the time of laparotomy. Cullen and others [2] have confirmed this observation.

Allen and Livingstone,[5] in a preliminary report on studies carried out on the human being, suggested that failure to establish an adequate prothrombin reserve before operation is probably a significant factor in causing the postoperative reduction of prothrombin in these patients.

In this paper data are presented which extend and confirm our previous report.

PRESENTATION OF DATA

In table 1 are compiled data obtained on 97 patients who were subjected to major surgical procedures other than operations on the biliary

TABLE 1.—*Prothrombin Studies on Nonjaundiced Surgical Patients*

Number of Patients	Anesthesia	Period of Anesthesia, Min.			Prothrombin, %	
		Maximum	Minimum	Average	Preoperative	Postoperative
38	Ethylene-oxygen	210	15	65	100	100
20	Ether	300	20	75	100	100
17	Procaine hydrochloride (local)	60	15	30	100	100
16	Spinal	75	22	45	100	100
14	Nitrogen monoxide	180	20	45	100	100
9	Vinethene	21	8	15	100	100
4	Splanchnic	90	55	70	100	100

tract and on 9 patients who underwent minor operations. In none of these patients was there any evidence of jaundice, poor fat absorption or disease of the liver. The anesthetic agents used are listed in the order of frequency in which each was employed in this study. Prothrombin determinations [6] were made in the case of each patient preoperatively and were repeated daily for at least four days during the postoperative period. In only 1 case was a reduction in prothrombin observed. In this case two surgical procedures were carried out on consecutive days with ethylene-oxygen anesthesia over a four-hour period on the first day and a three and one-half-hour period on the

4. Lord, J. W., Jr.: Effect of Trauma to the Liver on the Plasma Prothrombin, Surgery **6**:896, 1939.

5. Allen, J. G., and Livingstone, H.: Studies on the Early Postoperative Reduction of Promthrombin in the Jaundiced and Biliary Fistula Patient, with Special Reference to Anesthesia, Anesthesiology **1**:89, 1940.

6. Allen, J. G.; Julian, O. C., and Dragstedt, L. R.: The Use of Serial Dilution in the Determination of Prothrombin by the One-Stage Technique, Arch. Surg. **41**:873 (Oct.) 1940.

second day. On the second day icterus associated with oliguria and hyperpyrexia developed, and the patient died on the fourth postoperative day, apparently in acute hepatic failure. Autopsy was not permitted.

Studies on loss of blood [7] were carried out on 11 of the patients listed in table 1 and on 1 patient from the group listed in table 3. The surgical procedure and the estimated quantity of blood lost are presented in table 2. The volumes of blood lost varied considerably, ranging from 785 to 175 cc. Again, in only 1 patient was a reduction in prothrombin observed. That patient (case 12), who suffered from numerous abscesses of the liver, had a preoperative prothrombin deficiency which did not respond to vitamin K and bile salt therapy. There was no further significant reduction in prothrombin up to the time of death from septicemia, on the second postoperative day.

TABLE 2.—*Loss of Blood and Prothrombin Studies Made on Nonjaundiced Patients Subjected to Operation*

Case	Procedure	Blood Loss, Cc.	Prothrombin, %	
			Preoperative	Postoperative
1	Hysterectomy	480	100	100
2	Neck dissection	260	100	100
3	Mastectomy	785	100	100
4	Cervical laminectomy	695	100	100
5	Lobectomy	475	100	100
6	Mikulicz resection	360	100	100
7	Sarcoma of abdominal wall	560	100	100
8	Combined abdominoperineal resection	620	100	100
9	Subtotal gastrectomy	375	100	100
10	Panlaryngectomy	475	100	100
11	Lumbar laminectomy	685	100	100
12	Abscess of liver	175	58	55

Table 3 presents data obtained on 13 patients with obstructive jaundice and on 2 patients with biliary fistula. Preoperative vitamin K therapy, with 2-methyl-1, 4-naphthoquinone and bile salts, was instituted and elevated the level of plasma prothrombin to normal in each patient before operation was performed. The daily dose of naphthoquinone and the number of days that this drug was administered preoperatively to each patient are indicated in the table. The level of plasma prothrombin was determined daily for each patient during both the preoperative and the postoperative period. To none of the patients in this group was any vitamin K administered during the postoperative period until after a definite drop in the prothrombin level appeared. If by the fourth postoperative day no reduction in prothrombin occurred and the patient was taking food by mouth and if adequate bile salts were available for intes-

7. Gatch, W. D., and Little, W. D.: Amount of Blood Lost During Some of the More Common Operations, J. A. M. A. **83**:1075 (Oct. 4) 1924.

tinal absorption, further prothrombin studies were made at irregular intervals until the tenth day, when these determinations were discontinued. In every patient any prothrombin deficiency encountered during the postoperative period responded rapidly to vitamin K and bile salt

TABLE 3.—*Data on Patients with Corrected Prothrombin Deficiency, Showing the Correlation Between the Duration of Preoperative Vitamin K Therapy and the Length of Time During the Postoperative Period Before a Reduction in Prothrombin Appeared*

Case	Diagnosis	Anesthetic	Period of Anesthesia, Min.	Prothrombin, %		Vitamin K, Mg.	Days Given	Day Prothrombin Fell
				Initial	Preoperative			
1	Stone in common duct	Procaine hydrochloride (spinal) and ethylene-oxygen	210	45	100	8	7	7
2	Stricture of common duct	Nupercaine and ethylene-oxygen	90	15	100	8	5	5
3	Fistula of common duct	Procaine hydrochloride (spinal) and ethylene-oxygen	100	55	100	8	5	6
4	Stricture of common duct	Nupercaine and ethylene-oxygen	75	100	100	?	21	19
5	Stone in common duct	Procaine hydrochloride (spinal) and ethylene-oxygen	65	43	100	8	1	2
6	Stone in common duct	Procaine hydrochloride (spinal) and ethylene-oxygen	95	63	100	8	4	5
7	Carcinoma of pancreas	Nupercaine and nitrogen monoxide-oxygen	100	33	100	8	3	3
8	Stone in common duct	Procaine hydrochloride (spinal) and nitrogen monoxide-oxygen	110	28	100	8	5	6
9	Biliary fistula	Ethylene-oxygen	250	35	100	8	2	1
10	Stone in common duct	Procaine hydrochloride (spinal) and nitrogen monoxide-oxygen	235	100	100	8	1	1
11	Stone in common duct	Ethylene-oxygen and ether	145	66	100	8	4	4
12	Carcinoma of head of pancreas	Nupercaine (spinal)	90	28	100	8	2	1
13	Stricture of common duct	Ethylene-oxygen and ether	195	61	100	8	1	2
14	Carcinoma of head of pancreas	Ethylene-oxygen and ether	65	56	100	8	2	3
15	Stone in common duct	Nupercaine (spinal) and ethylene-oxygen	150	82	100	8	1	1

therapy, returning to normal within twenty-four hours after the administration of these compounds.

COMMENT

The role of the anesthetic agent employed for these patients does not appear to be a significant factor in the production of postoperative hypoprothrombinemia. The reduction was observed in patients subjected to

spinal anesthesia as well as those subjected to general anesthesia. Likewise, none of the 106 patients who underwent surgical procedures other than operations on the biliary tract gave evidence of postoperative hypoprothrombinemia except 1, who had probable acute hepatitis and died.

The question still unanswered is: Might not the already damaged liver be more susceptible than the normal liver to the potentially toxic effects of anesthesia? Recently, Allen, Kable and Livingstone [8] studied the effects of ether, ethylene, nitrogen monoxide, divinyl ether (vinethene) and cyclopropane administered with oxygen to dogs in which the prothrombin content of the plasma had been reduced by initial chloroform anesthesia. None of these five anesthetics, even when given on consecutive days to an animal with hypoprothrombinemia and hepatic insufficiency, produced any further reduction of prothrombin or retarded the return of hepatic function, as indicated by the return of the value for prothrombin to normal within five to seven days after the chloroform anesthesia. We have made similar studies on 3 patients with cirrhosis and prothrombin deficiency who did not respond to vitamin K therapy. In none of these patients was a further reduction in prothrombin encountered when they were subjected to operations carried out with general anesthesia. While so small a series does not permit a conclusion on this point, it suggests that even when the liver is damaged sufficiently to produce hypoprothrombinemia subsequent surgical procedures and anesthesia probably do not produce a further reduction of prothrombin.

The data in table 2 would seem to indicate that loss of blood encountered at the time of operation probably is not a major factor in the development of postoperative hypoprothrombinemia. These studies on loss of blood, carried out on 11 patients with normal channels for bile excretion and without apparent hepatic disease, revealed losses ranging from 260 to 785 cc. but showed no hypoprothrombinemia. In a previous report [5] we described a patient who was subjected to a subtotal gastrectomy. By the twelfth postoperative day the value for prothrombin had fallen to 28 per cent, probably as a result of repeated aspirations of contents of the upper part of the intestinal tract. Within four hours after the prothrombin level of 28 per cent was observed the patient had a massive emesis of blood. A posthemorrhagic prothrombin determination did not disclose any further reduction of the prothrombin concentration as a result of the hemorrhagic episode. Further studies on similar patients are necessary before final conclusions on the effects of loss of blood per se can be drawn.

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8. Allen, J. G.; Kable, V., and Livingstone, H.: Effects of Anesthetic Agents on Prothrombin Concentrations in Experimental Animals, Anesth. & Analg., to be published.

From the data thus far discussed it would appear that neither the surgical procedure and its accompanying loss of blood nor the anesthetic agent administered, exclusive of chloroform, presents an acceptable explanation for the postoperative hypoprothrombinemia. However, the postoperative reduction of plasma prothrombin in the patient with jaundice or a biliary fistula can be accounted for on the basis of inadequate preoperative vitamin K therapy. Table 3 clearly indicates that there is a close correlation between the period during which vitamin K is administered preoperatively and the number of days before the onset of postoperative hypoprothrombinemia. The longest period before the prothrombin level declined occurred in a case of jaundice due to stricture of the common duct. In this case an unknown quantity of vitamin K with bile salts was given for three weeks before the patient entered the hospital. At operation drainage of the right hepatic duct was done, which still permitted no flow of bile into the gastrointestinal tract, and it was nineteen days before any reduction in prothrombin appeared. Likewise, those patients receiving the least amount of vitamin K therapy showed the earliest appearance of the postoperative hypoprothrombinemia. As may be seen from the data in cases 10 and 11, even when no initial reduction in plasma prothrombin appears an early reduction may rapidly occur in the absence of preoperative therapy.

The close correlation between the amount of preoperative vitamin K therapy and the period which elapsed before a postoperative reduction appeared confirms our original postulate, namely, that inadequate preoperative administration of vitamin K is the most important single factor in the production of postoperative hypoprothrombinemia. This concept would imply that the vitamin in some form or prothrombin or one of its precursors can be stored within the body. The site of storage seemingly is the liver, since a sharp reduction rapidly follows the removal of this organ in the dog.[3]

At present there is no experimental evidence concerning the storage of either vitamin K or prothrombin. There is, however, some evidence available from patients with external complete biliary fistulas. We have observed the prothrombin levels in the cases of 2 patients who had postoperative biliary fistulas. In 1 case (case 3, table 3), two and one-half months elapsed before a reduction in the level of plasma prothrombin was observed, while in the other (case 9, table 3) four months elapsed before hypoprothrombinemia appeared. In each the value for prothrombin returned to normal within twenty-four hours after the administration of vitamin K–bile salt therapy. As soon as a normal prothrombin level was obtained, administration of these drugs was discontinued, and in each case the prothrombin level fell within two days. These studies were repeated several times, the duration of vitamin

K–bile salt therapy being varied, and it was found that the longer the period of administration of vitamin K and bile salts, the longer the prothrombin could be maintained at normal levels after the discontinuance of these drugs. This, we believe, is presumptive evidence that either prothrombin or vitamin K can be stored within the body, but of course further studies are necessary before any final conclusion can be drawn.

SUMMARY

Prothrombin studies were made on 106 patients who underwent surgical procedures exclusive of operations on the biliary tract. Except in 1 case, no change was found in the prothrombin levels following these procedures when ether, vinethene, nitrogen monoxide, ethylene-oxygen, avertin with amylene hydrate, nupercaine, spinal, or local anesthesia was used.

Loss of blood encountered at operation was determined on 11 patients who underwent surgical procedures other than operations on the biliary tract. As much as 785 cc. of blood was lost without reducing the level of plasma prothrombin.

Thirteen patients with obstructive jaundice and 2 patients with bile fistulas received preoperative vitamin K therapy for correction of prothrombin deficiency; in all but 2 of these patients, however, a sharp drop in prothrombin occurred during the postoperative period despite the correction of the initial prothrombin deficiency.

The suggestion is made that some form of storage of vitamin K or prothrombin probably occurs within the body and that the failure to replenish this store in the patient with obstructive jaundice or biliary fistula probably accounts for the postoperative hypoprothrombinemia seen in such patients.

CONCLUSIONS

The postoperative hypoprothrombinemia seen in the patient with obstructive jaundice or biliary fistula is the result of inadequate preoperative vitamin K–bile salt therapy and not the result of the usual anesthetic agents employed, exclusive of chloroform.

Eli Lilly & Co. supplied the 2-methyl-1, 4-naphthoquinone and the bile salts used in this study. The vinethene was supplied by Merck & Co.

CONGENITAL ELEVATION OF THE SCAPULA

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Although congenital elevation of the scapula was described in 1863 by Eulenburg,[1] the name of Sprengel,[2] who reported 4 cases in 1891 and who thought that his was the first description of the condition, commonly is given to the deformity. Sprengel's report was preceded also by an excellent description of a case, including autopsy observations and an interesting discussion of the significance of the omovertebral connection, by Willet and Walsham [3] in 1880. They reported a second case in 1883.[4] Since then the condition has attracted much attention, and many interesting papers have been written about it, notably those by Horwitz,[5] Grieg [6] and Schrock.[7] Apparently little remains to be added to the knowledge of the subject except development of a more satisfactory method of treating the deformity.

There can be little doubt that this is a true congenital deformity due to a defect in development of the embryo. A thorough description of the embryologic development of the upper extremity was published by Lewis [8] in 1902 and was summarized by Keibel and Mall [9] in their

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From the clinic of the New York Orthopaedic Dispensary and Hospital.

1. Eulenburg, M.: Beitrag zur Dislocation der Scapula, Amtl. Ber. ü. d. Versamml. Deutsch. Naturf. u. Aerzte (1862) **37**:291-294, 1868.

2. Sprengel: Die angeborenen Verschiebung des Schulterblattes nach oben, Arch. f. klin. Chir. **42**:545-549, 1891.

3. Willet, A., and Walsham, W. J.: Congenital Malformation of the Spinal Column, Bony Thorax, and Left Scapular Arch, Med.-Chir. Tr., London **63**:256-301, 1880.

4. Willet, A., and Walsham, W. J.: A Second Case of Malformation of the Left Shoulder Girdle, with Remarks on the Probable Nature of the Deformity, Brit. M. J. **1**:513-514, 1883.

5. Horwitz, A. E.: Congenital Elevation of the Scapula: Sprengel's Deformity, Am. J. Orthop. Surg. **6**:260-311, 1908.

6. Grieg, D. M.: Congenital High Scapula, with Which Is Included a Consideration of Brevicollis, Edinburgh M. J. **31**:22-44, 1924.

7. Schrock, R. D.: Congenital Elevation of the Scapula, J. Bone & Joint Surg. **8**:207-215, 1926.

8. Lewis, W. H.: The Development of the Arm in Man, Am. J. Anat. **1**:145-183, 1901-1902.

9. Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910, vol. 1.

"Manual of Human Embryology." Keith [10] gave a useful chronologic table of the development of various structures in the upper extremity, which was cited by Grieg. From these sources it appears that the upper limb bud develops as a mass of undifferentiated mesoderm in the cervical region during the fourth week. Early in the fifth week the condensation of the scleroblastema of the bud has extended to the distal part, and the anlages of the scapula, humerus, radius and ulna are distinguishable. In the 11 mm. embryo the scapula is composed of precartilage surrounded by a dense blastema, and it lies opposite the lower four cervical and the upper one or two dorsal vertebrae. In the 14 mm. embryo the scapula is well developed and is composed mostly of cartilage. It has migrated caudalward, so that less than half of it lies above the first rib. Keith stated that the scapula begins to descend from the neck to the thorax at the ninth week and reaches its ultimate thoracic position at the beginning of the third month. These facts make it evident that the high position of the scapula in persons with this deformity is determined very early, at a time when the embryo is so small that it is inconceivable that any external pressure from an abnormal position in utero or deficient amniotic fluid could have any influence.

An interesting feature of this condition is the presence in a certain number of cases of a structure connecting the scapula and the cervical portion of the spine. Horwitz observed this in 34 cases, or 25 per cent of his series, and it was noted in 14 of the 50 cases in this study. One's interest is at once aroused in the origin and significance of this structure, which may be bony, cartilaginous or fibrous. It arises from the upper portion of the vertebral border of the scapula and is joined usually to one or more of the lower cervical spinous processes and laminas, most often the fourth to the seventh.

A very large bony mass of this sort was found in Willet and Walsham's first patient, who died and on whom they performed an autopsy. This observation excited their curiosity, and they discussed it with Parker,[11] who was an authority on the comparative anatomy of the shoulder girdle. The position and form of this bone at once suggested to him its identity with the suprascapular bone of some of the lower vertebrates. This occurs in the frog and in the toad as a large osseous dorsal appendage of the scapula, which is not, however, united to the vertebral column. In the thornback skate a suprascapular bone exists which is firmly united both to the vertebral column and to the

10. Keith, A.: Human Embryology and Morphology, ed. 5, Baltimore, William Wood & Company, 1933.

11. Parker, W. K.: A Monograph on the Structure and Development of the Shoulder Girdle and Sternum in the Vertebrata, London, Robert Hardwicke, 1868.

scapula, forming a rigid pectoral girdle. In man and in the higher vertebrates the suprascapular bone is represented simply by the epiphysis at the vertebral border. This explanation of the occurrence of this

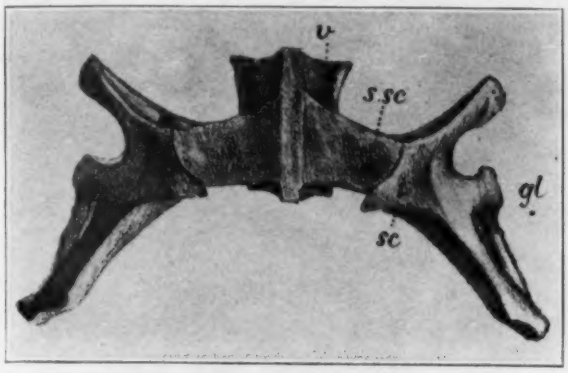

Fig. 1.—Suprascapular bone of the thornback skate, dorsal view. (From Parker.[11])

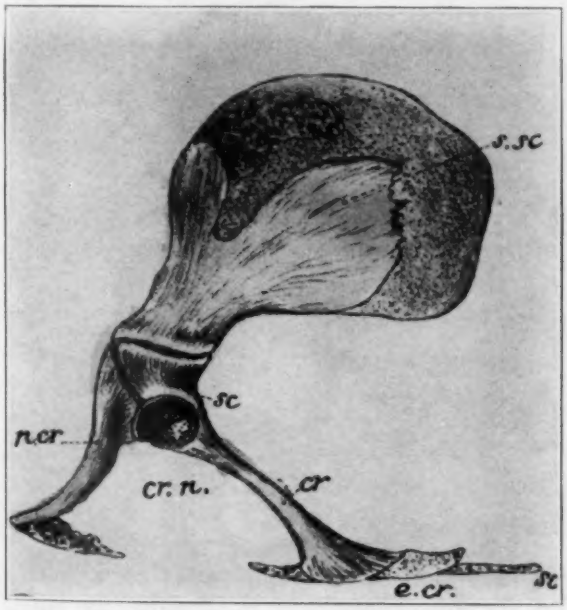

Fig. 2.—Suprascapular bone of the frog, lateral view. (From Parker.[11])

unusual structure in man seems to me to be the most logical and the one most in accord with the known facts.

Fifty cases were made the basis of this study. While too few to be of real statistical value in themselves, they may be a useful addition

to those previously reported. The patients were seen at the New York Orthopaedic Dispensary and Hospital from 1912 to 1939. In some of the earlier cases the data were not as complete as could be desired. The subjects varied in age from 1 month to 31 years, and the average age at admission was 5.5 years. Twenty-seven were females and 23 were males. The deformity occurred on the right side in 23 and on the left in 20 and was bilateral in 6. It was severe in 27, moderately severe in 10, slight in 4 and not noted in 9.

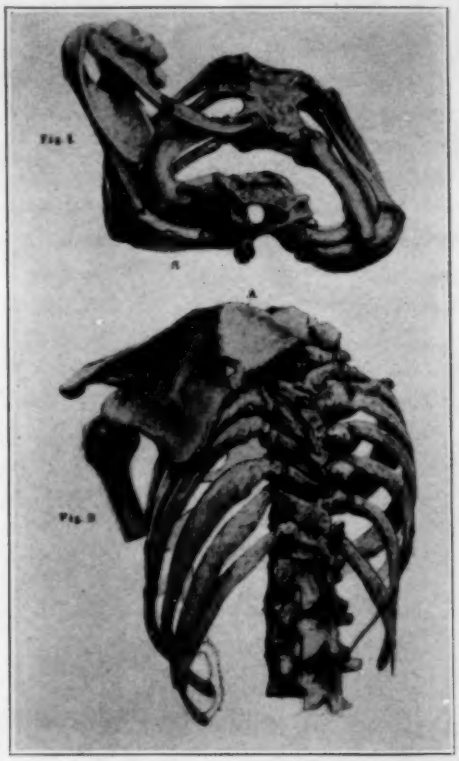

Fig. 3.—Autopsy specimen in Willet and Walsham's first case. (From Willet and Walsham.[3])

Associated congenital deformities of other parts of the body were present in 27 patients, which tends to confirm the thesis that high scapula is a true congenital abnormality. Of greatest frequency was the combination of malformation of the vertebrae in the cervical and upper dorsal regions, with lateral curvature of the spine and malformation and fusion of several ribs. This was found in 8 patients and was of serious import in relation to the high scapula, because the curvature in itself tended to elevate the shoulder and to interfere with attempts

to lower the position of the scapula. Malformation of vertebrae without lateral curvature was found in 4, and 6 had fusion of two or more ribs without defects in the spine. There were 6 patients with cervical ribs.

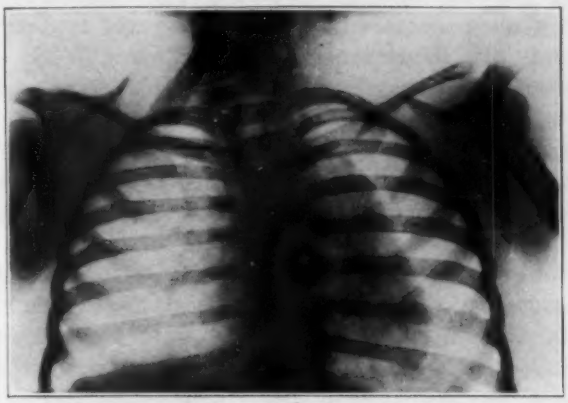

Fig. 4.—Roentgenogram showing congenital elevation of the scapula, with an omovertebral bone.

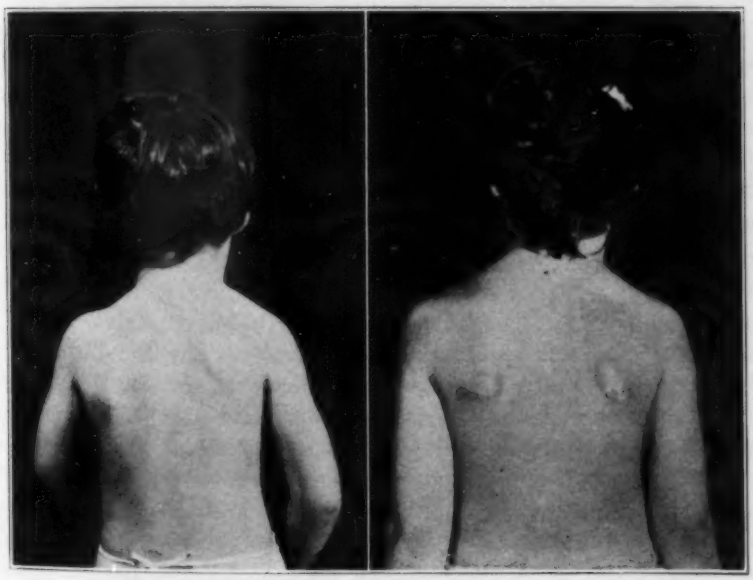

Fig. 5.—Photographs of a patient with congenital elevation of the scapula, before and after operation. Extensive subperiosteal release of the scapula was done.

The association of the last-mentioned condition with congenital elevation of the scapula was explained by Grieg by the theory that the normal suppression of the rib elements in the cervical region is an effect of

caudad migration of the upper extremity and the resulting pressure of the nerves as they are pulled downward. When the extremity fails to descend to its usual level, the pressure is not exerted to the same degree. Brevicollis, or short neck, was found in 1 patient and torticollis in 1. More remote congenital deformities occurred in 3 patients. No other deformity than the elevated scapula was found in 23.

Some connection between the high scapula and the spinal column was found in 14 patients, and none was noted in 36. Since this structure usually is covered by the rhomboid muscles, is difficult to palpate and in some cases is not easily demonstrated in a roentgenogram, it is quite possible that it was present but escaped detection in some of these patients. It consisted of a rhomboid osseous structure in 11 cases and of a fibrous band in 3. In the former group the bone was attached to the upper portion of the vertebral border of the scapula by cartilage in 10 and by a true joint in 1. Its connection to one or more of the lower cervical spinous processes and laminas was either by cartilage or by complete bony union. The phylogenetic significance of this structure has been discussed. Its practical importance lies in its effect in limiting the motion of the scapula and in interfering with efforts to lower it.

Of the patients in whom this point was noted, abduction of the arm was markedly limited in 17, moderately or slightly limited in 12 and not limited in 4. Of 12 patients who had an omovertebral connection the limitation of abduction was marked in 9 and moderate or slight in 3. Of 21 who had no such connection, limitation was marked in 8 and moderate, slight or absent in 13. Furthermore, the most severe grades of limitation were observed in those patients who had this structure.

Operations were performed on 14, or 28 per cent, of the 50 patients. One of the procedures was done at another hospital before the patient was admitted to this clinic. Operation was not advised for 12, was refused by 5 and is to be done subsequently on 2. In 17 cases the patient was followed for only a short time, and the question was not discussed. The operative procedures may be classed in three groups: 1. Simple removal of the omovertebral bone or fibrous band without extensive release of the scapula or any serious effort to lower it. 2. Extensive subperiosteal dissection of the scapula from its attached muscles; removal of the omovertebral bone, if present, and excision of a large portion of the scapula, including the spine and all of the bone above it, but without any attempt to anchor the bone in a lower position. 3. Extensive subperiosteal dissection of the scapula; removal of the omovertebral bone, if present; excision of only a small part of the supraspinous portion, if any, followed by pulling the scapula down to a much lower level and suturing it to a rib.

1. Removal of an omovertebral bone was carried out successfully by Willet in 1883. It was done as the chief operative procedure in 2 cases of this series. In 2 others a fibrous band connecting the scapula with the spine was excised. In 1 of the patients, from whom an omovertebral bone was said to have been removed by another surgeon when the patient was 6 months of age, it still was present when she was examined at this clinic. In only 1 of the 4 cases in which operation was confined to removal of the bone was abduction markedly limited before operation. The result was a substantial improvement in motion. In the others the gain was slight. An omovertebral bone was removed in 3 other cases as part of a more extensive operation. In 2 of these, in which there had been marked limitation of abduction before operation, there was a subsequent increase in this range.

2. Extensive subperiosteal stripping of muscles from the scapula and removal of a large portion of the bone, including the spine and supraspinous portion, was undertaken in 4 patients. This was done in an effort to make the shoulder less conspicuous, although no attempt was made to lower the position of the remainder of the scapula. An omovertebral bone was removed in 2 of these cases. In all of the members of this group the deformity was marked. Some improvement in the upper line of the shoulder at the junction with the neck resulted in 3 cases. In the fourth there was little, if any, gain. Any cosmetic improvement was offset in 2 cases by a wide scar and in a third by marked posterior projection of the lower angle of the scapula. It was necessary to operate a second time in 2 cases, in 1 to remove a spur which grew at the superior angle and in another to excise a fibrous band which developed at the site of an omovertebral bone. Abduction was increased in 2 patients in whom it was markedly limited before operation. It is fair to state that 1 case was made difficult by a lateral curvature due to malformation of the spine.

3. Freeing of the scapula from its muscles by subperiosteal dissection and anchoring it at a lower level by suturing it to a rib, was practiced in 5 patients, of whom 4 had severe and 1 moderately severe deformity. This is essentially the operation described by Schrock and Robertson. In 1 case the supraspinous part of the scapula was cut off, and in another an omovertebral bone was removed. No bone was excised in the remaining 3. In the first patient of this group the scapula had returned to its original position at the end of two and one-half years, and there was no improvement in abduction. The release of the scapula at the time of operation probably was insufficient. In a second case, much of the correction had been lost four years later, and there was marked winging of the scapula when the arm was pushed forward. The scar was conspicuous. In a third case the patient showed excellent maintenance of correction and marked improvement in appearance at the end

of four years. One of these patients exhibited complete paralysis of the extremity after operation. This was thought to be due to excessive traction on the brachial plexus in the presence of a hemivertebra with a lateral curve and fused ribs. Four years later the paralysis had been completely recovered from except for slight weakness of the serratus anterior muscle. A large degree of correction of the deformity had been retained, and abduction of the shoulder had increased from 120 to 160 degrees. The last patient had lost part of the correction at the end of seven months but still was improved. Some calcification had occurred in the bed of the omovertebral bone, but this had not become reattached to the spine.

SUMMARY

The embryologic development of the scapula and upper extremity and the significance of the omovertebral bone in terms of comparative anatomy are discussed.

The physical findings in 50 cases of congenital high scapula, including associated deformities, are given.

The results of 13 operations of various types for congenital elevation of the scapula are described. An increase in abduction of the shoulder was obtained in 3 cases by removal of an omovertebral bone. Attempts to improve the appearance of the shoulder by resection of a large portion of the scapula were disappointing. In 3 of 5 cases radical freeing of the scapula and suturing it to one of the lower ribs resulted in cosmetic and functional improvement.

CONCLUSIONS

1. Congenital elevation of the scapula is the result of a true defect in the embryo. The omovertebral structure which occurs in about 25 per cent of these cases is a homologue of the suprascapular bone which is found in several of the lower vertebrates.

2. In many cases of congenital elevation of the scapula the cosmetic and functional defects are not of sufficient severity to warrant any operation.

3. In cases in which an omovertebral bone is associated with marked limitation of abduction at the shoulder, improvement in function may be obtained by removal of the bone.

4. In certain cases of marked elevation of the scapula, improvement in appearance and function may be had by extensive subperiosteal release of the scapula and retaining the bone in a lower position by suturing it to a rib. The operation is fraught with difficulty, however, and the result may be impaired by several complications.[12]

12. D. E. Robertson, in a personal communication, reported that one of his patients had paralysis of the brachial plexus following operation, from which there was complete recovery.

FRACTURES AND DISLOCATIONS OF THE CERVICAL PORTION OF THE SPINE

WITH A REVIEW OF EIGHTY-NINE CASES

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The cases studied were 17 from private practice and 72 from the orthopedic and neurologic services of the Los Angeles County Hospital. For statistical purposes they are regarded as one series.

INCIDENCE

Estimating the number of patients with fractures who passed through the orthopedic services at 14,000 (a conservative figure) in three years, the 72 patients with fracture-dislocation of the cervical portion of the spine admitted in the same three year period made only 0.5 per cent of the total.

The majority (50.5 per cent) of the patients were in the age group from 20 to 39, and 79.7 per cent of them were men. The youngest was a baby of 7 months who had a fall on the head followed by paralysis and death; autopsy showed subluxation of the atlas. The oldest was a man of 72 who recovered from an automobile accident in which he sustained a dislocation of the sixth cervical vertebra anterior to the seventh.

This may be compared with an incidence of 82.5 per cent men in Soto-Hall and Haldeman's [1] series of 40 cases and 79.7 per cent men in a series of 79 cases collected from the general literature. Patients from 20 to 39 years of age made up 40 per cent and 43 per cent respectively of these two series.

CAUSE

A great variety of trauma contributes to the causation of these lesions. Dislocation alone may occur with very slight trauma or none at all, as is evidenced by many cases of subluxation resulting from inflammatory weakening of muscles and ligaments of the cervical region, notably of the first and second vertebrae (Brookes and Ewerhardt; [2]

1. Soto-Hall, R., and Haldeman, K. O.: Bilateral Dislocation of Cervical Spine, California & West. Med. **45**:238, 1936.

2. Brookes, T. P., and Ewerhardt, F. H.: Reducing and Treating Cervical Dislocation, Arch. Phys. Therapy **13**:463, 1932.

Hess, Bronstein and Ableson;[3] Frank[4]). Congenital anomalies of the vertebrae, such as absence of the odontoid process (Roberts[5]), may constitute a predilection to dislocation. Mechanisms producing slight trauma, such as sneezing, coughing or sudden twisting of the head, are listed under muscular violence.

Several cases have been reported in which dislocation was found after manipulation by an osteopath or a chiropractor (Blaine;[6] Jacobs;[7] Brookes[8]). None of this type was found in this series.

TABLE 1.—*Incidence*

Sex:	
Male	79%
Female	21%
Age:	
Under 10	3.5%
10 to 19	10.5%
20 to 29	20.4%
30 to 39	21.1%
40 to 49	14.1%
50 to 59	11.7%
60 to 69	5.8%
70 up	3.5%

TABLE 2.—*Cause*

Motor vehicles	57.9%
Fall	23.8%
Fighting, wrestling	6.8%
Dive	3.4%
Blow	1.1%
Muscular violence	1.1%
Not stated	5.7%

As for all other fractures, accidents with motor vehicles were responsible for the majority (59.7 per cent) of the fractures in this series.

3. Hess, J. H.; Bronstein, I. P., and Ableson, S. M.: Atlanto-Axial Dislocation Unassociated with Trauma and Secondary to Inflammatory Foci in the Neck, Am. J. Dis. Child. **49**:1137 (May) 1935.

4. Frank, I.: Spontaneous (Non-Traumatic) Atlanto-Axial Subluxation, Ann. Otol., Rhin. & Laryng. **45**:405, 1936.

5. Roberts, S. M.: Congenital Absence of the Odontoid Process, Resulting in the Dislocation of the Atlas on the Axis, J. Bone & Joint Surg. **15**:988, 1933.

6. Blaine, E. S.: Manipulative (Chiropractic) Dislocations of the Atlas, J. A. M. A. **85**:1356 (Oct. 31) 1925.

7. Jacobs, C. M.: Atlas and Axis Luxation, Am. J. Orthop. Surg. **16**:357, 1918.

8. Brookes, T. P.: Dislocation of Cervical Spine, J. Missouri M. A. **27**:579, 1930.

SYMPTOMS AND FINDINGS

The patient with the neck hyperflexed and the chin down on the chest probably has a bilateral dislocation. If the head is tilted to one side and rotated to the opposite side, there is usually a unilateral dislocation. Fracture alone, except perhaps extreme compression of two or more vertebral bodies, may not produce any visible deformity. Pain is not a prominent symptom, but tenderness on motion of the head and neck is pronounced. Difficulty in opening the mouth is suggestive of rotary dislocation of the atlas.

Neural symptoms may vary from slight tingling in the fingers to complete motor and sensory paralysis from the shoulders down. Loss of the sense of pain in the great toe is a sign of complete lesion of the spinal cord, since the fibers which convey this sensation go up the center of the cord (Stuck [9]). Fever, respiratory difficulty and priapism may all be present in cases of high lesions with damage to the cord.

TABLE 3.—*Symptoms*

	Paralysis 26.1%	Anesthesia 21.5%	Unconsciousness 35.2%
I	13%	5%	12.9%
II			19.3%
III			3.2%
IV	13%	10.5%	12.9%
V	39.1%	52.6%	16.1%
VI	34.8%	31.6%	29%
VII			6.5%

A dislocation at the fourth cervical vertebra or above, with involvement of the cord, may produce paralysis of all four extremities; if the lesion is at the level of the fifth cervical vertebra the upper parts of the arms may be spared; if it is at the level of the sixth cervical vertebra only the legs can be paralyzed. If sensation persists, motor function may return (Crutchfield [10]). Spasticity and increased reflexes are promising signs when present at first (Voris [11]).

In Roberts' [12] series, symptoms of compression of the cord were present with 75 per cent of the fractures and with only 10.5 per cent of the dislocations. In my series, 26.1 per cent of the patients were

9. Stuck, R. M.: Spinal Cord Compression Injuries, Broken Necks and Broken Backs, with Spinal Cord and Spinal Nerve Injury, J. Kansas M. Soc. **40**: 48, 1939.

10. Crutchfield, W. G.: Fracture-Dislocation of Cervical Spine, Am. J. Surg. **38**:592, 1937.

11. Voris, H. C.: Treatment of Fracture and Dislocation of Cervical Spine, S. Clin. North America **17**:543, 1937.

12. Roberts, S. M.: Fracture and Dislocation of Cervical Spine, J. Bone & Joint Surg. **19**:477, 1937.

paralyzed. Dislocation alone produced the paralyses in 8 instances, fracture alone in 5 and fracture-dislocation in 10. The site of the lesion as shown in the roentgenogram did not always correspond to the site of the lesion in the cord as shown by the neurologic findings. For example, in 4 cases in which the osseous lesion was at the level of the sixth cervical vertebra there was, nevertheless, complete paralysis of all four extremities. This may be explained by assuming that the lesion of the cord extended upward from the osseous lesion or that there was another lesion of the cord at a higher level.

Analysis of the cases of paralysis showed that in 13 it was complete, of all limbs; in 5, of the legs only; in 1, of the arms only; in 2, of one arm; in 2, hemiplegia, and in 1, of the Brown-Séquard type. Except in 3 cases of dislocation of the first cervical vertebra all the paralyses were caused by lesions of the fourth, the fifth or the sixth cervical vertebra, the injuries being about equally divided among dislocations, fractures and fracture-dislocations. Table 3 shows that there was no paralysis or sensory disturbance from lesions at the level of the second or of the third cervical vertebra. This is explained by the fact that at the level of the second and the third cervical vertebra the bony canal is larger in proportion to the size of the cord than it is at the lower cervical levels.

Loss of sensation was noted in a smaller percentage (21.5 per cent) of the cases than was loss of motion. In 35.2 per cent of the series unconsciousness immediately followed the accident and lasted from a few minutes to a few hours.

The dislocations were all anterior except 1; that is, the superior vertebra was anterior to the adjacent one below it. Considering the structure of the vertebra, it is obvious that a posterior dislocation, unless complicated by fracture, could not persist long enough to be demonstrated by roentgen examination. An anterior dislocation persists only if the superior vertebra overrides the inferior vertebra far enough so that the articular facets lock. In a few instances, especially in rotary dislocations of the first cervical vertebra over the second, the inferior facet of the upper vertebra may catch on top of the superior facet of the lower, but usually with these subluxations there is spontaneous reduction. This probably accounts for the cases in which severe neurologic symptoms occur without demonstrable lesions of bone.

In the 1 case of posterior dislocation in this series, there was a fracture of the anterior part of the body of the fifth cervical vertebra with a posterior displacement of the posterior part of the body, enough to impinge on the cord. Complete paralysis below the waistline and death in three days resulted.

SITE OF LESIONS

The sixth cervical vertebra was involved in more cases than any other, and in 49.4 per cent the lesion was in either the fifth or the sixth cervical vertebra. This disagrees with the statement in some textbooks that the third cervical vertebra is the weakest part of the cervical portion of the spine. There was no case of isolated fracture of the atlas, but there were 6 of dislocation and 5 of fracture-dislocation of this vertebra. According to del Rosso,[13] isolated fracture of the atlas is very rare; a fracture of the skull and/or a fracture of the axis is usually present also. No compression fracture of the body of a vertebra was found

TABLE 4.—*Site of Lesions*

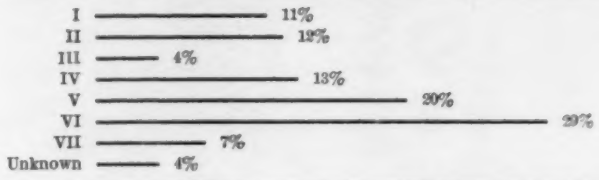

TABLE 5.—*Site of Classified Lesions*

	Fractures 43%	Dislocations 31%	Fractures and Dislocations 22%
I	.....	19.3%	22.7%
II	18.6%	3.2%	13.6%
III	4.6%	3.2%	4.5%
IV	13.9%	22.6%	
V	20.9%	19.3%	22.7%
VI	27.9	29%	36.4%
VII	13.9%	3.2%	

above the fifth cervical vertebra. Dislocations alone were found to be more frequent (22.5 per cent) in the first two cervical vertebrae than fracture alone (18.6 per cent). Combined fracture and dislocation involved these two in 36.3 per cent. In Soto-Hall and Haldeman's [1] series 55 per cent of the lesions were in the fifth and sixth cervical vertebrae. In Brookes's [14] series of 90 cases of dislocation alone, 57.7 per cent of the lesions were located at the level of the first and second cervical vertebrae. Blasius [15] (84 cases) found the fifth and sixth involved in 52.3 per cent.

13. del Rosso, L. M.: Sopra due casi di frattura "isolata" dell'atlante, Chir. d. org. di movimento **17**:325, 1932.

14. Brookes, T. P.: Fracture and Dislocation of Cervical Spine, J. A. M. A. **109**:6 (July 3) 1937.

15. Blasius, cited by Warshaw, D.: Dislocation of Cervical Spine: Case of Complete Forward Dislocation of VI C with Reduction by Forcible Traction and Full Recovery, Ann. Surg. **99**:470, 1934.

As is noted in table 6, the body of the vertebra was the part most frequently involved in fractures. This is the easiest part to demonstrate by roentgen examination, while the laminas and the pedicles may sometimes escape detection. This may in part account for the 4 per cent "unknown" in table 3. The other excuse for these unknown sites is that the patient had all the clinical symptoms of a lesion of the cervical part of the spine but died in shock before roentgen examination could be made.

TREATMENT

In 37.5 per cent of this series the only treatment was extension of the head followed by use of an ambulatory cast or a brace. Manipulation followed by application of a cast was done in 6.8 per cent, and a cast only was used in 15.9 per cent. Skeletal traction was applied in 5.7 per cent. In a number of cases, 17 per cent, the treatment was expectant, meaning usually that the patient was in such a serious condition that not much could be done to the local lesion. Another 17 per cent must be recorded under "treatment not known," owing to deficiency in the hospital records.

TABLE 6.—*Parts Involved in Fractures*

Body of vertebra	51.5%
Spinous process	21.2%
Odontoid process	13.6%
Lateral mass	6.1%
Pedicle	3%
Lamina	3%
Articular process	1.5%

Reduction of dislocations may be accomplished in many cases by extension alone. However, in cases of severe or complete paralysis an attempt should be made as early as possible to reduce the dislocations by manipulation. There may be cases of immediate and complete paralysis due not to destruction of the cord but to compression by a wide dislocation. If this compression is allowed to persist for several hours, irreparable destruction of the cord may follow, with the result that the patient is more or less a cripple for life. Given a patient with complete and immediate paralysis, skilful manipulation and manual extension at once at the scene of the accident may relieve pressure and preclude permanent paralysis. No time should be consumed with a trip to an emergency hospital, a transfer to a general hospital and then a wait for roentgen examination. In view of the foregoing statistics, if there is paralysis the chances are that the lesion is at the fourth cervical vertebra or below, and one does not take much risk of respiratory

failure or other fatal result in manipulating a spine with a lesion at this level and keeping the neck in extension from the start. An emergency temporary head halter can be made out of a 3 inch (7.5 cm.) muslin bandage and two safety pins, and with this halter an ambulance man can hold the head in extension on the way to the hospital. Once in bed at the hospital, the patient should not be moved, but roentgenograms should be taken with a portable machine. One patient who walked after falling on his head and who had a gradual development of paralysis the next day died while he was being moved to have a roentgenogram taken. In another case, a boy of 15 twisted his neck in a fall in a gymnasium

Fig. 1.—*A*, roentgenogram showing dislocation of the fifth over the sixth cervical vertebra in a man aged 24. Successful reduction was accomplished by manipulation. Dislocation recurred in three months. The final condition was as shown. There were no symptoms. *B*, roentgenogram of a patient with complete paralysis and anesthesia from the neck down following a fall on the head. There was a slight fracture of the fourth cervical vertebra but no roentgen evidence of pressure on the cord.

and became unconscious. He "came to" in a few minutes and was allowed to walk to the dressing room, where he became unconscious again. He was then taken to a hospital and put to bed, where after gentle manipulation he became conscious again. Roentgen examination after the manipulation gave negative results.

The Walton [16] manipulation was used more frequently than the Taylor [17] method in this series. Reduction of the dislocation is a procedure which requires more skill than force, and by the former method delicate control can be maintained. The forcible extension which is the essence of the Taylor method may be necessary for some bilateral lesions. Walton devised his method in the pre-roentgen-ray days and based his plan on observations at the autopsy table. He called it retrolateral flexion without extension. He held that forcible extension is not only unnecessary but actually may hinder reduction by preventing action of the fulcrum mechanism on the opposite side while one side is being reduced.

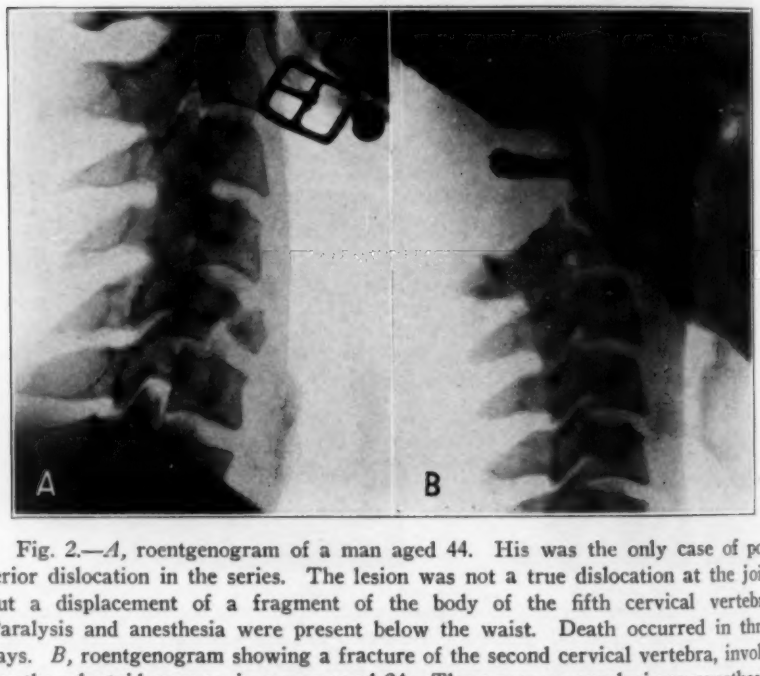

Fig. 2.—*A*, roentgenogram of a man aged 44. His was the only case of posterior dislocation in the series. The lesion was not a true dislocation at the joint but a displacement of a fragment of the body of the fifth cervical vertebra. Paralysis and anesthesia were present below the waist. Death occurred in three days. *B*, roentgenogram showing a fracture of the second cervical vertebra, involving the odontoid process, in a man aged 24. There was no paralysis or anesthesia. The patient collapsed during application of skeletal traction and died nine hours later.

No open reductions, fusions or laminectomies were done in this series, although some such procedure might have been indicated in at least 2 cases. In 1 of these there was a recurrence of dislocation of the

16. Walton, G. L.: Further Observation on Cervical Dislocation and Its Reduction, Boston M. & S. J. **149**:445, 1903.

17. Taylor, A. S.: Fracture-Dislocation of Cervical Spine, Ann. Surg. **90**:321, 1929.

fifth cervical vertebra about two months after a successful reduction by manipulation. In the other, the patient removed his plaster collar himself and at once had a recurrence of a dislocation of the fourth cervical vertebra. Voris [11] stated that manipulation with the patient under anesthesia probably gives a higher mortality than laminectomy. However, in our series there was no death which could be attributed to manipulation alone, with or without anesthesia.

In a few cases manipulation was unsuccessful, and dislocation without paralysis persisted. In 1 case the patient was not seen until five weeks after the accident. Since there were no neural symptoms, a dislocation of the sixth cervical vertebra was allowed to persist because the patient refused to submit to manipulation, wishing to let well enough alone. At present, eight years later, he takes long mountain hikes and other strenuous exercise in spite of evident torticollis resulting from the persisting dislocation.

The application of skeletal traction is delegated to the brain surgeons. The Crutchfield tongs is the apparatus of choice for this. Crutchfield [10] gave credit to Coleman as the first to use skeletal traction on the skull in 1932. Cone and Turner [18] at a meeting of the American Orthopedic Association in Toronto, Canada, in July 1932, reported several cases in which they had used skeletal traction by means of wires through drill holes in the skull. Later they reported 12 cases of fusion after reduction by skeletal traction, stating that dissection in this region is done with an electrocautery to avoid trauma. Crutchfield [19] reported 42 cases of treatment with skeletal traction up to 25 pounds (11.3 Kg.). In all 27 cases in which he treated the injury within two months complete reduction was obtained. One advantage of the Crutchfield tongs is that the patient can be turned on the side easily without disrupting the extension apparatus.

Wiring of the spinous processes to prevent recurrence of dislocation has been done by Ryerson and Christopher,[20] Cotton,[21] Lane,[22] Speed,[23] Osgood [24] and others, with varying success. The difficulty with this

18. Cone, W., and Turner, W. G.: The Treatment of Fracture-Dislocation of the Cervical Vertebrae by Skeletal Traction and Fusion, J. Bone & Joint Surg. **19**:584, 1937.

19. Crutchfield, W. G.: Treatment of Injuries of the Cervical Spine, J. Bone & Joint Surg. **20**:696, 1938.

20. Ryerson, E. W., and Christopher, F.: Fracture of Cervical Vertebrae: Operative Correction, J. A. M. A. **108**:468 (Feb. 6) 1937.

21. Cotton, cited by Ryerson and Christopher.[20]

22. Lane, cited by Ryerson and Christopher.[20]

23. Speed, cited by Ryerson and Christopher.[20]

24. Osgood, cited by Ryerson and Christopher.[20]

method seems to be that the bone of the spinous processes is not dense enough to stand the strain, and the wire pulls out.

Dislocations of the upper cervical vertebrae require long-continued immobilization, with support of the head to insure against recurrence and a fatal result. Osgood and Lund,[25] reporting fractures of the odontoid process, advised immobilization for six months and stated that manipulation is dangerous in these cases. They called attention to the fact that the odontoid process is stronger than the anterior arch

Fig. 3.—Roentgenogram of a boy aged 17. There were symptoms of dislocation of the upper part of the cervical portion of the spine. A developmental anomaly was present; there was failure of the odontoid process to fuse with the second cervical vertebra. The symptoms subsided after a week in extension.

of the atlas but weaker than the articular ligament which encircles the odontoid process posteriorly. Jefferson,[26] in a report of 4 cases of fracture of the atlas, stated that if this condition is not recognized and reduced it may cause death due to a sudden increase of dislocation of the fragments. Open reduction may be necessary for this fracture.

25. Osgood, R. B., and Lund, C. C.: Fractures of the Odontoid Process, New England J. Med. **198**:61, 1928.

26. Jefferson, G.: On Fractures of the First Cervical Vertebra, Brit. M. J. **2**:153, 1927.

Hudson [27] found that conservative extension methods without operation were successful in 45 cases which he reported. King [28] advised skeletal traction if anesthesia and paralysis are present. Oppel [29] removed an entire anterior arch of a fractured atlas and obtained improvement of symptoms. Bonnet [30] advised postponing fusion operations for two or three months to avoid operative accidents. He stated that he uses local anesthetics. Pybus [31] successfully reduced an anterior dislocation of the fifth cervical vertebra by open operation and direct leverage, approaching the anterior aspect of the spine by lateral incision and postpharyngeal dissection. Craig [32] removed the posterior arch of the first cervical vertebra and the posterior margin of the foramen magnum with the region under local anesthesia to relieve gradually developing compression myelitis. The patient recovered to normal. Spinal fusion was done in all of 18 cases of fracture-dislocation of the lower cervical vertebrae reported by Cole.[33] Langworthy [34] reported 30 cases of dislocation, in 13 unilateral and in 17 bilateral, in all of which the dislocations were reduced by the Walton method, mostly with the patient under general anesthesia. Casts were applied at once with the spine in hyperextension.

RESULTS

The general mortality of the entire series was 25.8 per cent. Of the 23 patients who died, 15, or 65.2 per cent, had lesions of the fifth and/or the sixth cervical vertebra. Table 1 shows that 49 per cent of the lesions were of the fifth and/or the sixth cervical vertebra, so that the mortality from involvement of these two vertebrae is greater than that noted for any of the others. Only 20 per cent of the patients with lesions of the first and/or the second cervical vertebra died. Most of the deaths, 73.9 per cent, occurred in the first five days; 39.1 per cent, in the first twenty-four hours.

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27. Hudson, O. C.: Fractures and Dislocations of the Cervical Spine, J. Bone & Joint Surg. **17**:324, 1935.

28. King, T.: Some Difficulties in the Treatment of Dislocation of the Cervical Spine, Australian & New Zealand J. Surg. **6**:380, 1937.

29. Oppel, W. A.: Anterior Subluxation of the Atlas, Lancet **1**:698, 1927.

30. Bonnet, G.: Deux observations de "dislocation atlo-axoïdienne" sans troubles bulbo-médullaires. Echec du traitement orthopédique: Verrouillage de sûreté par greffe d'Albee, Bull. et mém. Soc. nat. de chir. **59**:1296, 1933.

31. Pybus, F. C.: Fracture-Dislocation of the Cervical Spine and Its Open Reduction, Brit. M. J. **2**:860, 1936.

32. Craig, W. M.: Fracture-Dislocation of the Cervical Vertebrae Without Injury to the Spinal Cord, S. Clin. North America **11**:841, 1931.

33. Cole, J. P.: Dislocation and Fracture-Dislocation of the Lower Cervical Vertebrae, Arch. Surg. **35**:528 (Sept.) 1937.

34. Langworthy, M.: Dislocation of Cervical Spine: Thirty Cases, J. A. M. A. **94**:86 (Jan. 11) 1930.

As might be expected, the mortality among patients with complete paralysis was high. Of the 18 with paralysis of three or more limbs, 13 (72.2 per cent) died, all within nine days except 1 man, who lived forty-four days. One patient with complete and immediate paralysis is living after eight years, still paralyzed from the neck down. He showed only a mild compression of the sixth cervical vertebra in the roentgenogram; the damage to the cord may have been caused by a dislocation which reduced itself spontaneously. The neurologic consultant advised against operation on the ground that the cord was beyond repair. Another man totally and immediately paralyzed by a fall on the head and shoulders is living after three years. A bilateral dislocation was reduced within three hours by the Walton method with the patient under general anesthesia. On coming out of the anesthetic he could move his hands and made further improvement under weight extension. He is now spastic, walks a little with help, feeds himself, has fair biceps but no triceps power and has trouble with the bladder.

Manipulation was successful in 55.5 per cent of the cases in which it was tried. In 22.2 per cent the position was improved, and in 22.2 per cent manipulation failed to reduce the dislocation. There was recurrence of the dislocation after good reduction in 3.3 per cent.

In fractures, there was never much change in the position of the fragments after extension. In 1 case the displaced body of the second cervical vertebra could be felt with the fingers through the mouth, but it did not yield to gentle pressure combined with extension of the head; neither did it show any change after five weeks under traction with Crutchfield's tongs. The patient still wears a support after nine months and has never had any neurologic symptoms.

Crutchfield [19] reported that 80 per cent of patients with hopeless lesions of the cord died within ten days. The mortality in 45 cases reported by Hudson [27] was 13.3 per cent. Roberts [35] reported 21 cases, with 19 per cent mortality. It is interesting to note that in the preroentgen days the mortality records were much higher, 77 per cent (Ashhurst [36]) and 92.6 per cent (Blasius [37]), the explanation being that only the serious lesions were recognized. For the atlas alone, Jefferson [38] reported a mortality rate of 54 per cent, and for fracture of the odontoid process Osgood and Lund [25] reported 50 per cent mortality. In a total of 59 cases from the literature, the mortality was 10.1 per cent.

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35. Roberts, S. M.: Dislocation of Cervical Spine, J. Bone & Joint Surg. **19**: 199, 1937.

36. Ashhurst, cited by Cole.[33]

37. Blasius, cited by Cole.[33]

38. Jefferson, G.: Fractures of the Atlas Vertebra, Brit. J. Surg. **7**:407, 1920.

CONCLUSIONS

The study of these cases suggests that in some instances severe and permanent paralysis might have been avoided if a reduction of the dislocation could have been done earlier. Perhaps one should do more laminectomies for lesions which are usually considered hopeless. When complete paralysis exists but no interference with the neural canal can be demonstrated by roentgen examination, it may be that the cord is not completely severed but that edema inside the dura is causing a block which could be relieved by laminectomy and longitudinal incision of the dura. The patient has nothing to lose and everything to gain from operation.

VERTEBRAL COMPRESSION FRACTURES SUSTAINED DURING CONVULSIONS

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It is well known that muscular action alone can break bones, such as the femoral neck [1] or the bones of the forearm.[2] However, fractures of vertebral bodies by muscular action, except in cases of tetanus, were practically unknown until recently, after the advent of convulsive shock therapy, although such fractures have been reported to have occurred in breeding stallions. The question of fractures from convulsive spasms has assumed more importance since inauguration of convulsive shock therapy for the psychoses. Since the introduction of shock therapy in 1935, occasional fractures have been reported by various observers; however, many of the fractures were overlooked because of the mildness or absence of symptoms. In the early days of convulsive shock therapy, no roentgenograms were taken unless the symptoms called for the procedure; recently roentgen examination has been routinely employed by one of us (S. A.) before and after treatment in all cases of convulsive shock therapy. In this communication a report is made of 7 vertebral compression fractures sustained during convulsions induced by metrazol in a group of 30 patients. These fractures occurred in 6 men and 1 woman between the ages of 28 and 50; the condition of 6 had been diagnosed as schizophrenia, and that of 1, as manic-depressive phychosis. Each patient received between seven and twenty injections of metrazol and responded with moderate or severe convulsions. Three of the patients did not complain of any symptoms suggestive of a fracture; 3 others complained of tenderness and pain in the region involved, radiating along the spinal nerve roots, which lasted from three days to two weeks; in 1 of the patients the discomfort lasted for over a year,

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1. Baish: Ueber chronischen Tetanus, München. med. Wchnschr. **65**:127, 1918. Androp, S.: Bilateral Fracture of the Femoral Necks Caused by Metrazol Convulsions, J. Nerv. & Ment. Dis., to be published.

2. Wilhelm, T.: La cyphose tétanique, J. de chir. **22**:295, 1923.

necessitating constant wearing of a corset. In 1 of the patients the patellar reflexes became unequal, the inequality lasting about ten days. The onset was sudden, the convulsion lasting on the average one minute and passing through a succession of clonic-tonic-clonic stages. The fractures sustained resembled those seen in cases of tetanus. The anterior part of the vertebra is almost always compressed, without apparent injury to the spinal cord, and the posterior part may remain intact. Figure 1 illustrates a typical vertebral compression fracture sustained during a convulsion induced by metrazol shock therapy. A brief review of the literature and a study of the mechanism of vertebral compression fractures sustained during convulsions will be presented.

Fig. 1.—Typical vertebral compression fracture sustained during a convulsion induced by metrazol shock therapy.

FRACTURES IN CASES OF TETANUS

Roberg [3] and others have reported a limited number of cases of vertebral fractures which were demonstrated roentgenographically after tetanus. A definite description of anatomic changes induced in vertebral bodies by tetanic convulsions has been made in only 3 cases.

FRACTURES IN CASES OF EPILEPSY AND OTHER CONVULSIVE DISORDERS

Although one would strongly suspect the occurrence of vertebral fractures due to muscular spasm during epileptic attacks, there is a

3. Roberg, O. T., Jr.: Spinal Deformity Following Tetanus and Its Relation to Juvenile Kyphosis, J. Bone & Joint Surg. **35**:603, 1937.

paucity of cases reported in the literature. Ziskind and Ziskind[4] reported 3 cases of fracture of the spine occurring during epileptic attacks and cited 3 other cases, reported by Rand. As we could find no other cases in the literature, it was deemed of much interest to examine the spines of a series of epileptic patients to see whether any of them showed vertebral fractures. A group of 50 patients from an epileptic colony with frequent severe grand mal seizures were selected, and their vertebral columns were roentgenographed anteroposteriorly and laterally. No sign of a vertebral fracture was observed in any of these patients. In a similar manner, several groups of patients suffering from convulsions on a syphilitic or an arteriosclerotic basis or due to cerebral neoplasms were examined and were found roentgenographically free from any signs of fractures in the vertebral column. No cases of vertebral fracture due to strychnine-induced convulsions or to eclampsia were found in the literature. From a review of the literature one is convinced that compression fractures of the vertebral column are by far more frequent with convulsive shock therapy than with any of the convulsive disorders. These fractures seldom occur in epileptic seizures or the other convulsive disorders, because the tonic stage is not as long and violent as in the attacks due to metrazol; the injury occurs during the tonic stage.

LOCATION OF FRACTURES

In convulsions due to shock therapy the fractures occur most frequently in the area from the fourth to the eighth thoracic vertebra, which is the region least covered by the spinal erector muscles and least resistant to a contraction of the musculature of the anterior part of the trunk. In cases of tetanus, fractures occur almost entirely in the region of the fourth to the sixth thoracic vertebra; only 2 occurred in the lumbar region. The very few reported as occurring in cases of epilepsy occurred in the tenth, eleventh and twelfth thoracic and in the second and third lumbar vertebrae. Ordinary compression fractures occur in the twelfth thoracic, the first lumbar and the fifth, sixth and seventh cervical vertebrae. According to Fick,[5] the fifth thoracic vertebra is the weakest in the entire spine.

SYMPTOMS OF FRACTURES

The usual symptoms indicating that fractures of the vertebrae have taken place are tenderness and pain of the affected area of the spine, radiating from the spinous processes along the spinal nerve roots. This

4. Ziskind, E., and Somerfeld-Ziskind, E.: Compression Fracture of the Spine in Epilepsy, Bull. Los Angeles Neurol. Soc. **4**:45, 1939.

5. Fick, R.: Handbuch der Anatomie und Mechanik der Gelenke unter Berücksichtigung der bewegender Muskeln, Jena, Gustav Fischer, 1911, vol. 3.

as a rule will disappear within a few days or a week. One of our male patients was compelled to wear a corset for over a year; another patient showed inequality in his patellar reflexes lasting only ten days.

POSSIBLE CAUSES OF FRACTURES

Restraint was mentioned by Palmer [6] as a predisposing cause of fractures; however, it was eliminated as a possible factor in our series. The patients were allowed perfect freedom of movement during the convulsions, with no interference from the nursing personnel. The treatments were administered in bed, and the patients were carefully guarded against a direct injury to the spine. The contributory effect of local circulatory disturbance should be considered, as should hypocalcemia, which first takes place in the bones of the vertebral column, which is most labile. Moffat [7] pointed out that pathologic fractures of the vertebrae resulting from loss of calcium from the spinal column are not uncommon and are, in the majority of cases, due to a faulty diet. He reported 10 cases. Although no determination of calcium balance was made in the group of cases of fractures due to metrazol therapy, there was nothing to suggest a background of disease or defect in the muscular system or in the skeleton. Although many still question the possibility of this occurrence in normal vertebral bodies, it has been generally impossible to find a predisposing condition. The age of the patient, apparently, is not a factor in this condition.

SEVERITY OF FRACTURES

All degrees of severity, from a severe crush to the slightest chip off the anterior rim or a small crack, are encountered. The type most frequently encountered with metrazol shock therapy is that due to compression of the anterior part of the vertebra, with or without involvement of the posterior part. The vertebral bodies are cancellous, with a rich blood supply; evidently compression fractures are accompanied by extravasation of the contents of the disk, with a consequent lessening of its height. This will be confirmed when the material comes to pathologic study. Roberg [3] claimed that roentgen determination of a fracture is not absolutely certain. Fragmentation of the bony structure extending through the periphery of the shadow is certain evidence of fracture. Displacement of one portion of the body against another body in a sagittal or a frontal direction also demonstrates a fracture. Flattening in a vertical direction or isolated wedge formation

6. Palmer, H. A.: Vertebral Fractures Complicating Convulsion Therapy, Lancet **2**:181-183, 1939.

7. Moffat, B. W.: Pathologic Fractures of the Spine Associated with Disorders of Calcium Metabolism, Arch. Surg. **28**:603 (June) 1934.

associated with a continuous line of increased density in the interior of the body, even in the presence of an intact outline, is suggestive of a break in the spongiosa. It is plausible that only a microscopic fracture may be present.

MECHANISM OF FRACTURES

Although the mechanism of fractures occurring during convulsions or muscular spasms is still not definitely established, it may be explained on the basis of the contraction of certain muscle groups during the convulsions. The typical postconvulsive shock therapy fracture of the thoracic vertebrae is caused by a predominating, severe contraction of the anterior musculature of the trunk, which produces anteflexion of the spine at this point. Radmann [8] explains the mechanism of spinal compression fractures as the result of muscular action incited by external trauma. Accordingly, the force of a jarring or bending fracture of the spine is not transmitted simply in a vertical direction from one body to another, but its horizontal and vertical components are resisted by a third component, represented by a sudden tension occurring in muscles fixed at a point anterior to the spine and contracting reflexly. The contraction of these muscles compresses the anterior surfaces of the bodies in a mechanism similar to that of tetanic curving of the thoracic portion of the spine anteriorly.

FORCE INVOLVED

The muscular contraction which causes a vertebral compression fracture is a force that cannot be estimated; it is not known what resistance a vertebral body makes to such a force, and the leverage which is transmitted by the ribs and in the bending of the spine on itself has not yet been measured. That the muscular contraction in convulsions due to metrazol shock therapy is of extreme severity is illustrated in figure 2, which shows a bilateral fracture of the femoral necks. This occurred at the height of the tonic stage, when a distinct snap was heard. Göcke [9] found that weights up to 480 Kg. did not alter the form of a vertebral body but, through condensation and increased brittleness of the spongiosa, diminished the resistance to compression and increased the elasticity of the bone after a certain time, so that the transient elastic flattening which at first occurred with each blow recovered less and less, and the vertebra became brittle and lost its initial resistance to sudden pressure. This is analogous to the loss of temper in iron through hammering and is a physical explanation for

8. Radmann: Zur Kenntnis der mittelbaren Wirbellbrüche, Beitr. z. klin. Chir. **129**:466, 1923.

9. Göcke: Traumatische Wirbelumformung in Versuch, in Hefte zur Unfallheilkunde, Leipzig, F. C. W. Vogel, 1931, p. 136.

diminished resistance of the vertebral body through transgression of the limit of elasticity without initial fracture of the spongiosa.

TRAUMA WITHOUT APPARENT FRACTURE

From physical and pathologic standpoints, where even a slight change has taken place in a vertebral body without alteration in form the affected bone is more exposed to damage by the normal daily burden. Where a change in shape has already taken place, the weakened link or bent portion throws the entire chain into static decompensation, and a more definite basis is provided for later changes. Roberg [3] maintained

Fig. 2.—Bilateral fracture of the femoral necks, sustained at the height of the tonic stage of a convulsion induced by metrazol shock therapy. A distinct snap was heard at the time of fracture.

that it is far more difficult for the roentgenologist than for the pathologist to separate a true fracture, associated with a single collapse and shattering of the bone trabeculae and hemorrhages, from a change in form of the vertebral body associated with a mere gradual transformation of the bone tissue. When a very evident fracture of the spine occurs, the action of the force is of such short duration that unless a fracture occurs at the time the vertebral column usually escapes without injury; however, such trauma can sometimes lead to progressive disintegration of the cancellous bone, as in Kümmell's disease, or to progressive vertebral atrophy.

FRACTURES APPARENTLY DUE TO DIRECT VIOLENCE

Although compression fractures of the vertebral column due to direct violence are not within the scope of this communication, the following case is reported because of some interesting features.

REPORT OF A CASE

A woman 61 years old, in the hospital for many years, suffering from schizophrenia, complained of pain in the back and tenderness in the lumbar region. Roentgen examination was indicated, which the patient refused, becoming combative, and the procedure was unsuccessful. A month later the patient still complained of pain and showed slight kyphosis. After a brief period of heavy sedation, a roentgenogram was taken, which revealed a moderate compression fracture of the eighth thoracic vertebra. The patient had not received any convulsive shock therapy, nor had she ever been seen in a state resembling a convulsion. Because the patient entertained delusions and at times had hallucination and because there had been no witnesses to the accident, the means of the injury was still obscure. The patient gave a vague account of sitting on the edge of the bed and said that some other patient, whom she was unable to identify, struck the bed forcibly, throwing her forward and thereby hurting her back. There were no visible marks anywhere on the body.

SUMMARY

The apparently normal adult vertebral column is susceptible to gross or microscopic compressed fractures under the influence of tetanic, epileptic and metrazol-induced convulsions.

Seven cases of vertebral compression fractures sustained by muscular action during convulsions induced by metrazol shock therapy for the psychoses are reported.

A brief review of the literature and a formulation of the mechanism of vertebral compression fractures occurring in the various convulsive disorders are presented.

EXTRA-ARTICULAR OSTEOSYNTHESIS

FOR NONUNION OF FRACTURE OF THE NECK OF THE FEMUR

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Although the bone graft is always mentioned in any discussion concerning the treatment of ununited fractures of the neck of the femur, it has been used for only a small percentage of patients afflicted with such fractures. At the Mayo Clinic only 1 in 10 of the patients who came with ununited fractures of the neck of the femur were subjected to a bone grafting procedure. The chief reason for the infrequent use of this type of operation is that most patients with ununited fracture of the neck of the femur are seen by the surgeon when the femoral neck is practically absorbed. Local conditions at the site of fracture being thus unfavorable and the open operation (intra-articular osteosynthesis) being too extensive and complicated to be employed indiscriminately for elderly patients, the use of the bone graft has been limited to a smaller group of younger, more robust patients.

I offer no new procedure to solve the problem. This paper is presented to show that the extra-articular employment of the bone graft in a selected group of cases is practical and, accompanied as it is with little or no danger, will serve to broaden the field of usefulness of the bone graft.

Many have contributed to the literature on the bone graft. Long ago, Albee [1] wrote of using a carefully prepared, rounded autogenous bone graft as a peg in ununited fractures of the neck of the femur. Campbell [2] reported 36 cases in which treatment was by the aid of the bone graft, with 5 unknown results, 1 death, 22 successes and 8 failures. King [3] has advised the use of a fibular graft reenforced by a Smith-Petersen nail. Gallie and Lewis [4] reported 15 cases in which treatment

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From the Section on Orthopedic Surgery, the Mayo Clinic.

1. Albee, F. H.: Treatment of Ununited Fracture of the Neck of the Femur, Surg., Gynec. & Obst. **49**:810-817 (Dec.) 1929.

2. Campbell, W. C.: Ununited Fracture of the Neck of the Femur, Surgery **1**:499-516 (April) 1937; Operative Orthopedics, St. Louis, C. V. Mosby Company, 1939.

3. King, T.: The Closed Operation for Intracapsular Fracture of the Neck of the Femur: Final Results in Recent and Old Cases, Brit. J. Surg. **26**:721-748 (April) 1939.

4. Gallie, W. E., and Lewis, F. I.: Ununited Fracture of Neck of Femur in Aged, J. Bone & Joint Surg. **22**:76-80 (Jan.) 1940.

was by means of extra-articular osteosynthesis with use of a bone graft and a nail, with union in 6 cases and failure in 1; in the remainder the patients were either in bed or on crutches, so that the end results were not determinable at the time of his report. Dickson [5] advocated the use of small multiple grafts obtained from the tibia after opening the joint and provided fixation with a Smith-Petersen nail.

I recently reported [6] a series of cases that represented an experience of twenty-six years (from July 1913 to June 1939) in which the bone graft was used for ununited fractures of the neck of the femur. There were 77 cases in all; the end results are now known in 71. Of these, the patients in 50, or 70 per cent, obtained bony union. There were 2 deaths, a mortality of 2.5 per cent, both due to emboli. In the 2 cases in which death occurred the results were classed as failures.

Extra-articular osteosynthesis can be performed with no surgical shock, and if local conditions are favorable (that is, if the head of the femur is viable and enough of the femoral neck is present) operation of itself carries little risk even for elderly patients. Because it is necessary to have the position of the fragments and of the guide wire determined by roentgen means, the operation, often prolonged and tedious, tries the patience of the surgeon. It is the type of operation that is easy for the patient but trying for the surgeon.

Prolonged postoperative fixation in a cast, which has been considered essential, is a drawback, but I am inclined to believe that most elderly persons tolerate such fixation much better than is generally thought. Nevertheless, the stiffness in the knee and hip that follows long fixation is decidedly undesirable. Undoubtedly it would be better if fixation in a cast were not necessary and early movement of the hip and knee could be instituted.

Compere and Lee [7] have reported 7 cases in which treatment was by the use of several bone grafts, with two or more screw wires in addition to give fixation and thus obviate the necessity for postoperative use of a cast. Six of their patients obtained bony union. This method has the great advantage of permitting early movement, the treatment being practically ambulatory. With such a procedure the question of damaging an already devitalized femoral head by placing in it one or more bone grafts and metal nails or screws is to be considered. In

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5. Dickson, J. H.: Treatment of Ununited Fractures of the Neck of the Femur by Means of Bone Graft and Smith-Petersen Nail, S. Clin. North America **19**:1235-1241 (Oct.) 1939.

6. Henderson, M. S.: Ununited Fracture of Neck of Femur Treated by Aid of Bone Graft, J. Bone & Joint Surg. **22**:97-106 (Jan.) 1940.

7. Compere, E. L., and Lee, J.: The Restoration of Physiological and Anatomical Function in Old Ununited Intracapsular Fractures of the Neck of the Femur, J. Bone & Joint Surg. **22**:261-276 (April) 1940.

1936 I used the lag screw in conjunction with the bone graft for 2 patients and obtained good results in both. They were held in a cast for six weeks before motion was permitted.

EXTRA-ARTICULAR OSTEOSYNTHESIS

The extra-articular method of osteosynthesis with the bone graft has been used for 14 patients at the Mayo Clinic, and my presentation concerns these patients. The average age of these 14 patients was 56 years, ten years greater than that in the group already referred to, in which treatment was by intra-articular osteosynthesis. This indicates that the surgeons were willing to undertake the risk of operation in a group of patients a decade older than when the extra-articular osteosynthetic method was used.

Requirements Preparatory to Extra-Articular Osteosynthesis.—Prerequisites to extra-articular osteosynthesis are: 1. The head of the

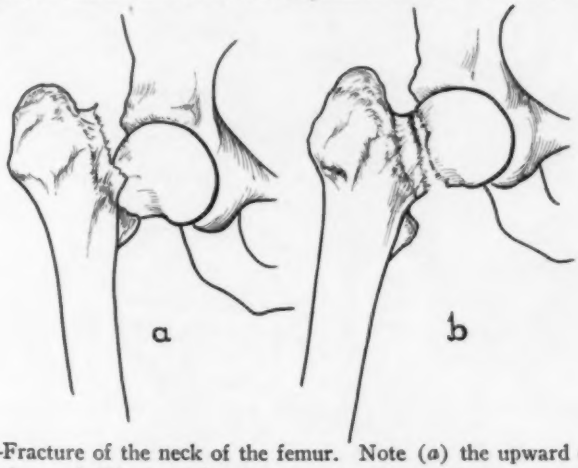

Fig. 1.—Fracture of the neck of the femur. Note (*a*) the upward displacement with shortening and (*b*) the deformity overcome by traction.

femur should have normal contour, and the roentgen findings should indicate a viable head. 2. A sufficient amount of the neck of the femur should still be present (at least a third to a fourth). 3. Complete correction of eversion must be obtained and the shortening overcome as much as possible (fig. 1). There should be roentgen evidence of proper alinement of the head and neck of the femur in anteroposterior and lateral views. Either cutaneous or skeletal traction in bed (cutaneous traction is usually sufficient) combined with maintenance of the foot and ankle in the upright position for a few days to several weeks is usually necessary (fig. 2). If such correction cannot be attained by preoperative traction, the extra-articular method should not be used. If the graft is placed with the head and neck of the femur in malalinement, the shear-

ing force during the convalescent period will be too great and the graft will break.

Technic.—With the aforementioned requirements fulfilled, with spinal or general anesthesia, through a lateral incision 3 or 4 inches (7.5 to 10 cm.) in length over the base of the trochanter where it meets the shaft of the femur (fig. 3 *a*), a Kirschner guide wire 3/32 inch (2.34 mm.) in diameter is inserted as nearly as possible through the center of the neck of the femur and the center of the head. The guide wires used in this clinic are all 30 cm. long. The depth to which the wire has been placed, therefore, can always be readily calculated by subtracting from 30 cm. the distance from the point at which the wire enters the bone to the exposed end of the wire. Roentgen studies are

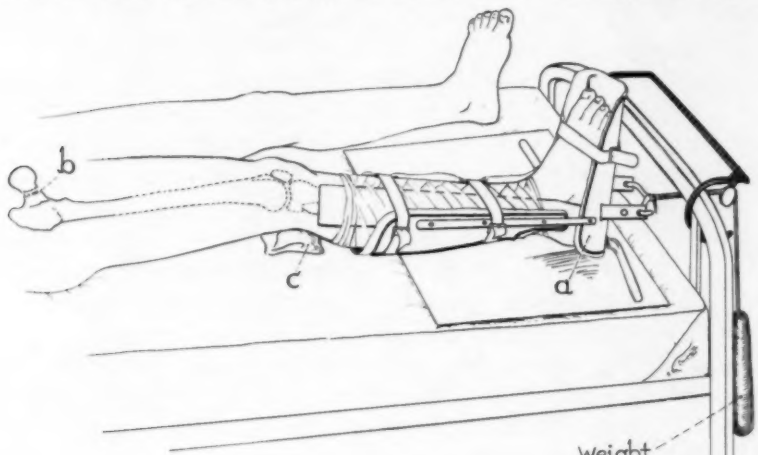

Fig. 2.—Traction maintained with a splint applied to overcome eversion. Note (*a*) the traction apparatus; (*b*) the fracture of the neck of the femur, and (*c*) the small pad to prevent hyperextension of the knee.

made anteroposteriorly and laterally to determine the position of the wire. If the position is correct, the wire is inserted deeply enough to engage the acetabular wall.

Over this guide wire, which is cut off so that it is 14 cm. in length (1 cm. short of the length of the opening of the drill), are threaded a series of cannulated drills (fig. 3 *b*), and a tunnel is made into the neck and head of the femur.

After the cannulated drills are threaded over the guide wire, the fibula on the same side is exposed in its middle third, and a segment of the proper length, usually 3½ to 4 inches (8.75 to 10 cm.), is removed. The fibula is approximately ½ inch (1.2 cm.) in diameter. This wound

should be closed immediately. The fibular graft is carefully cleansed of all muscle, and its surface is thoroughly freshened with a chisel (fig. 3 *c*).

The fibular graft is then threaded over the wire and is driven well into the head after a cannulated drill of the proper size had been used

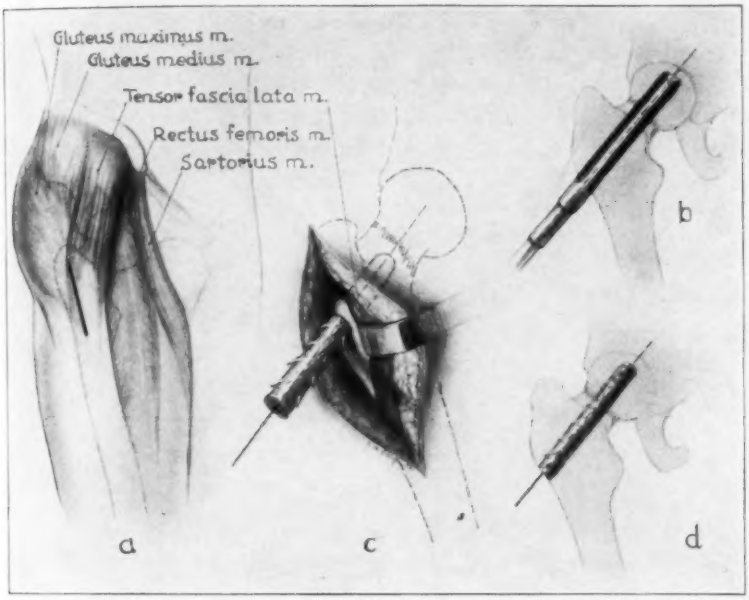

Fig. 3.—Anatomic relations of incision and bone graft. Note (*a*) the incision at the base of the trochanter; (*b*) the fibular bone graft cleansed of all muscle, thoroughly roughened and partially inserted in the tunnel prepared for it; (*c*) the cannulated drill inserted over a guide wire, and (*d*) the fibular bone graft in the proper position.

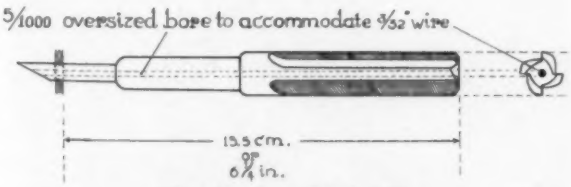

Fig. 4.—Cannulated drill.

to prepare the tunnel for its reception (fig. 3 *d*). A drill of the proper size should be selected in order to insure a snug fit of the bone graft in the tunnel. The fracture surfaces should then be thoroughly impacted by pounding, thus eliminating as much as possible a shearing force being applied to the graft in the course of convalescence.

The drills used here are made in the clinic's own shop of cold rolled iron, with the flutes not so deep as those of the standard types in order that an opening 3/32 inch (2.34 mm.) in diameter can be made for 16 cm. in the middle of these drills. This lumen is 0.005 inch (0.125 mm.) oversize (fig. 4). The drills are case hardened later. There are three sizes, 3/8, 1/2 and 5/8 inch (0.94, 1.25 and 1.56 cm.) respectively. Before the cannulated twist drill is put over the wire, the distance from the cortex of the femur to the end of the wire in the head must be determined, and the wire must be cut so that its total length will not exceed 14 cm. If it is longer than 14 cm., the drill will tend to push the wire through into the pelvis, an occurrence that has been

Data in Fourteen Cases of Extra-Articular Osteosynthesis for Nonunion of Fracture of the Neck of the Femur

Case	Duration of Nonunion, Months	Age, Years	Sex	Date of Operation	Type of Graft	Result *	Date of Last Observation
1	7	67	F	6/20/36	Fibular	Union (E)	4/40
2	8½	58	F	9/24/36	Fibular	Nonunion (P)	3/37
3	6	57	F	9/25/36	Fibular	Union (F)	11/38
4	10	43	F	10/27/36	Fibular lag screw	Union (E)	5/40
5	13	51	M	10/28/36	Fibular lag screw	Union (E)	4/40
6	10	64	M	4/ 6/37	Fibular	Union (E)	4/40
7	5	63	F	7/31/37	Fibular	Nonunion (P)	3/40
8	7	67	F	7/15/38	Fibular	Union (E)	6/40
9	10	52	F	9/21/38	Fibular	Union (E)	2/40
10	84	49	M	1/ 3/39	Fibular	Union (E)	5/40
11	3	57	F	1/10/39	Fibular	Union (G)	3/40
12	5	62	F	4/25/39	Fibular	Union (G)	4/40
13	4	46	F	10/12/39	Fibular	Union (E)	5/40
14	8	70	F	4/23/40	Fibular	Indeterminate †	Still under observation

* E, excellent; bony union with full function. G, good; bony union with good function. F, fair; bony union with poor function. P, poor; no union.
† Operation too recent to report results.

reported in the literature several times. It is well to remember that the canal in the center of the drill must be carefully cleaned so that no collection of debris will narrow its lumen. If the wire does not have free play in the canal, it will bind and will be forced inward into the pelvis. Pure phenol followed by alcohol should be poured through this canal before sterilizing as an additional precaution for asepsis.

An anteroposterior roentgenogram should be taken to make sure that the bone graft is set sufficiently deep in the head of the femur. Then the guide wire is removed.

Postoperative fixation must be provided by means of a spica cast of plaster of paris that holds the leg in slight abduction with the foot in the upright position. Every bone graft goes through a period of weakness and has no real strength until at least three months after insertion.

Fig. 5.—Nonunion of ten months' duration in woman aged 43 years.

Fig. 6.—Union three and a half years after operation. Note (*a*) the antero-posterior view and (*b*) the lateral view.

During this period the graft undergoes rarefaction and partial absorption; this is promptly followed by regeneration. Weight bearing should not be permitted until six months have elapsed.

Results.—There were 14 patients operated on by the extra-articular osteosynthetic method (see table); their average age was 56 years. Three were in the fifth decade, 5 in the sixth, 5 in the seventh and 1 in the eighth. Eleven were women and 3 men. There were no deaths or postoperative complications of any kind. Bony union was secured in 11 cases; of these, excellent results were achieved in 8, the patients having sufficient function for all practical purposes. Two had good function but still were unable to put on their own shoes and lace them. One had only fair function, with malunion and with the leg in eversion. In the cases of 2 there was utter failure, as the grafts and the state of nonunion persisted as before. One is still in the convalescent stage (figs. 5, 6 and 7).

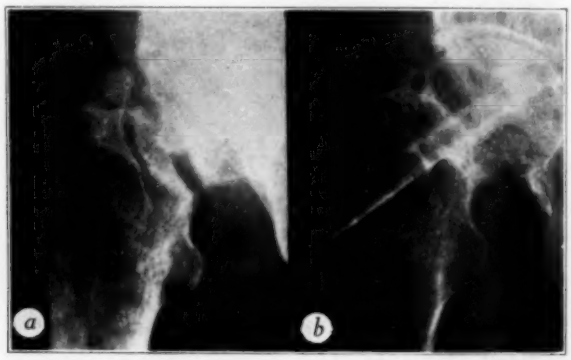

Fig. 7.—Nonunion of seven months' duration in a woman aged 67 years. The illustrations show (*a*) the appearance before operation and (*b*) the appearance two years after operation, with firm bony union.

Duration of Disability.—So many factors enter into the duration of disability that I finally gave up attempting to record the months of disability. The patients are elderly, and one therefore cannot expect too much in this respect. I am sure, however, that on the whole the duration of disability has been less and the residual stiffness of the knee and hip less in this group, in which operation was by the extra-articular method, than in the group in which the intra-articular method was used.

CONCLUSIONS

Extra-articular osteosynthesis carried out for 14 patients with nonunion of the neck of the femur has been done, with no danger to the patients comparable to that associated with the intra-articular method.

Bony union was secured in 11 of 13 cases in which sufficient time has elapsed to determine the end result. Eight of the patients had practically normal function; the function of 2 was classified as good, that of 2 as poor and that of 1 as fair. One is not far enough along in convalescence to allow accurate judgment of what the end result will be. It is my belief that this method materially broadens the field for the use of the bone graft. Perusal of the literature definitely shows that the bone graft gives the best results in such cases, and therefore it should be used when possible.

PERIOSTEAL FIBROSARCOMA

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Primary malignant tumors of bone constitute approximately 1 per cent of all types of malignant neoplasms.[1] Of this 1 per cent, an extremely small proportion is made up of periosteal fibrosarcomas. Kolodny,[2] in his review of the material in the Bone Registry of Sarcoma in 1928, found only a few cases. Geschickter and Copeland have stated that, among over 1,700 neoplasms involving bone, only 1.5 per cent were placed in this group. In a series of 200 primary malignant bone tumors seen at the University Hospital since 1925, comprising osteogenic sarcoma, Ewing's sarcoma, multiple myeloma and periosteal fibrosarcoma, 27 were included in the last-named group, a relatively high incidence. In every instance the diagnosis was made on the basis of a combination of clinical, operative, roentgen and histologic observations.

GENERAL CONSIDERATIONS

The age distribution in these 27 cases was, in general, that found in most cases of sarcoma. Twenty-one patients, or 78 per cent, were under 40 years of age. Approximately one-half the patients were in the second and third decades of life. The youngest patient was 1 year of age and the oldest 76. The average age was 32 years.

There were 17 males and 10 females, or 63 per cent and 37 per cent respectively.

There was a family history of some type of malignant tumor in 4 cases; in none of these was there a history of bone tumor. In 17 cases there was no family history of malignant tumor, and in 6 cases the history was not established.

In 10 cases, or 37 per cent, there was a history of trauma. In 4 of these the trauma initiated the symptoms and might well have merely called attention to a preexisting lesion. In 2 cases the trauma antedated the symptoms by ten years; hence there was probably no relation of cause and effect. In the remaining 4 cases the trauma preceded the

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1. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, ed. 2, New York, American Journal of Cancer, 1936.

2. Kolodny, A.: Bone Sarcoma, Chicago, Surgical Publishing Company of Chicago, 1927.

symptoms by intervals varying from three to twenty-seven months. From this analysis it is evident that trauma probably does not play an important role in the development of periosteal fibrosarcoma.

CLINICAL MANIFESTATIONS

The average duration of symptoms was twenty months, a relatively long period as compared with the duration of other types of primary

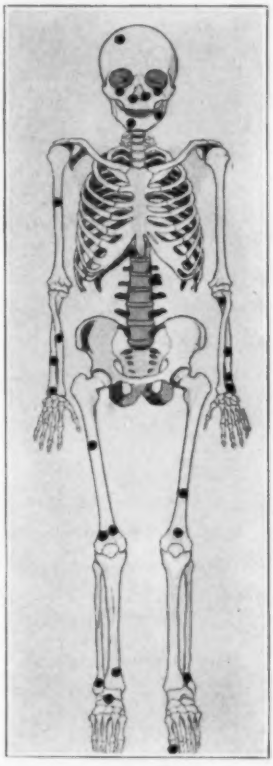

Fig. 1.—Distribution of periosteal fibrosarcoma in 27 cases.

malignant bone tumors. The shortest duration was one month; the longest was eight years. The outstanding symptoms were pain and swelling. In most instances the pain preceded the swelling, although in several cases the tumefaction was first noted. In 3 cases the presenting symptom was tumor formation without any history of pain. The pain was usually not severe, sometimes intermittent and often worse at night. The majority of patients at the time of admission to the hospital had no constitutional symptoms, such as ease of fatigue, loss of strength, anorexia or loss of weight. Four had metastases to the lungs on admis-

sion, with pain in the chest, cough, dyspnea and hemoptysis in addition to the generalized manifestations of far advanced cachexia. One patient had metastases to the regional lymph nodes on admission.

The tumor was typically deep seated, smooth and without fixation to the overlying tissues. It could be distinguished from lesions in the soft parts by its limited mobility due to its deep attachment to the periosteum. The tumor was usually firm, not hard and only moderately tender. Locally increased heat was not a marked feature. Dilatation of the superficial vessels, so often noted with osteogenic sarcoma and Ewing's sarcoma, was absent. When the tumor was in the neighborhood of a joint there was limitation of motion of that joint.

The distribution of the lesions is shown in figure 1. Without exception the lesions were single. The most common sites were the ulna and the femur, which were involved in 6 and 5 cases, respectively. The upper extremity was involved in 8 cases, or 30 per cent; the lower extremity, in 10 cases, or 37 per cent; the skull, in 7 cases, or 26 per cent; and the spine, in 2 cases, or 7 per cent. Of the lesions in the skull, 4 were in the maxilla, 2 in the mandible and 1 in the frontoparietal region. The lesions in the long bones showed a predilection, in the ratio of 5 to 3, for the ends of the bone as compared with the shaft, the distal end usually being involved.

ROENTGEN CHARACTERISTICS

The roentgen characteristics were largely determined by the changes in the underlying bone. These changes were of two main types, the destructive and the reactive. The more common type, the destructive, or lytic, showed a relatively large soft tissue tumor overlying an area of erosion in the contiguous cortex. The eroded area was usually smooth and involved one side of the shaft, indicating its extraosseous origin. In a few cases in which the lesions showed marked destructive changes in the bone it was impossible to rule out roentgenologically the presence of an osteolytic osteogenic sarcoma. Figure 2 illustrates the typical roentgen features of bone-destructive periosteal fibrosarcoma.

In cases of the reactive type of osseous lesion the only roentgen signs, in addition to the soft tissue swelling, were thickening and roughening of the underlying cortex, with little or no bone destruction. There was no true bone formation as seen in osteogenic sarcoma. Occasionally flakes of calcium could be seen in the substance of the tumor. Figure 3 illustrates this type of lesion.

PATHOLOGIC FEATURES

Periosteal fibrosarcoma arises from the fibrous layer of the periosteum, and the pathologic picture is similar to that of sarcoma arising from other connective tissue structures, such as fascial sarcoma. The

Fig. 2.—Typical roentgenogram of the bone-destructive type of periosteal fibrosarcoma.

Fig. 3.—Typical roentgenogram of the bone-reactive type of periosteal fibrosarcoma.

osseous changes are secondary, although occasionally they are so extensive that they overshadow the true soft tissue nature of the lesion. Grossly, the lesions at operation were found to be firm, generally encapsulated and white and glistening on cut section, with evident whorl formation. In cases of bone-destructive lesions, as seen in roentgenograms, there was disappearance of the underlying cortex with invasion of the medullary cavity, which usually showed hemorrhagic changes. In cases of lesions showing reactive osseous changes there was frequently a sharp line of demarcation between the substance of the tumor and the underlying roughened cortex; in these cases the tumor could be shelled out with ease, although the upper and the lower limits were not well defined.

The microscopic features of periosteal fibrosarcoma were essentially the same as those of any sarcoma of fibrous tissue origin. The histologic changes were a reflection of the degree of differentiation of the cells in the process of fibrogenesis. In the most highly differentiated group the appearance closely resembled that of a benign fibroma composed of cells approaching the fibroblast type, with an abundance of collagen fibers and definite whorl formation. The somewhat less differentiated and more malignant tumors showed a decreased proportion of fibers in which the whorl formation was not marked. The least differentiated and most malignant tumors were made up almost entirely of small, closely packed, hyperchromatic spindle cells with scarcely visible cytoplasm, showed frequent mitotic figures and had practically no intercellular substance. Geschickter and Copeland have classified tumors in the various stages of dedifferentiation as fibrosarcoma, fibrospindle cell sarcoma, spindle cell sarcoma and oat cell sarcoma, the last being the most malignant type. Meyerding and Broders [3] have distinguished three types, the fibrous, the fibrocellular and the cellular fibrosarcoma.

In this series no attempt was made to follow either of the aforementioned classifications. The plan of distinguishing four grades, as suggested by Broders, was used, grade 1 indicating the lowest degree and grade 4 the highest degree of malignancy. The principal criteria for grading were the degree of cell differentiation, the number of mitotic figures and the relative proportions of cells and intercellular substance. Microscopic sections for grading were available in 21 cases and, as classified by Dr. Lloyd F. Catron, gave the following results: grade 1, 2 cases; grade 2, 10 cases; grade 3, 8 cases, and grade 4, 1

3. Meyerding, H. W.; Broders, A. C., and Hargrave, R. L.: Clinical Aspects of Fibrosarcoma of the Soft Tissues of the Extremities, Surg., Gynec. & Obst. **62**:1010-1019 (June) 1936.

case. The objection so often raised to the grading of malignant tumors, particularly sarcomas, that various grades are present in the same tumor, has much less force with regard to this type of lesion, because, as Broders has pointed out, the structure of fibrosarcoma is usually

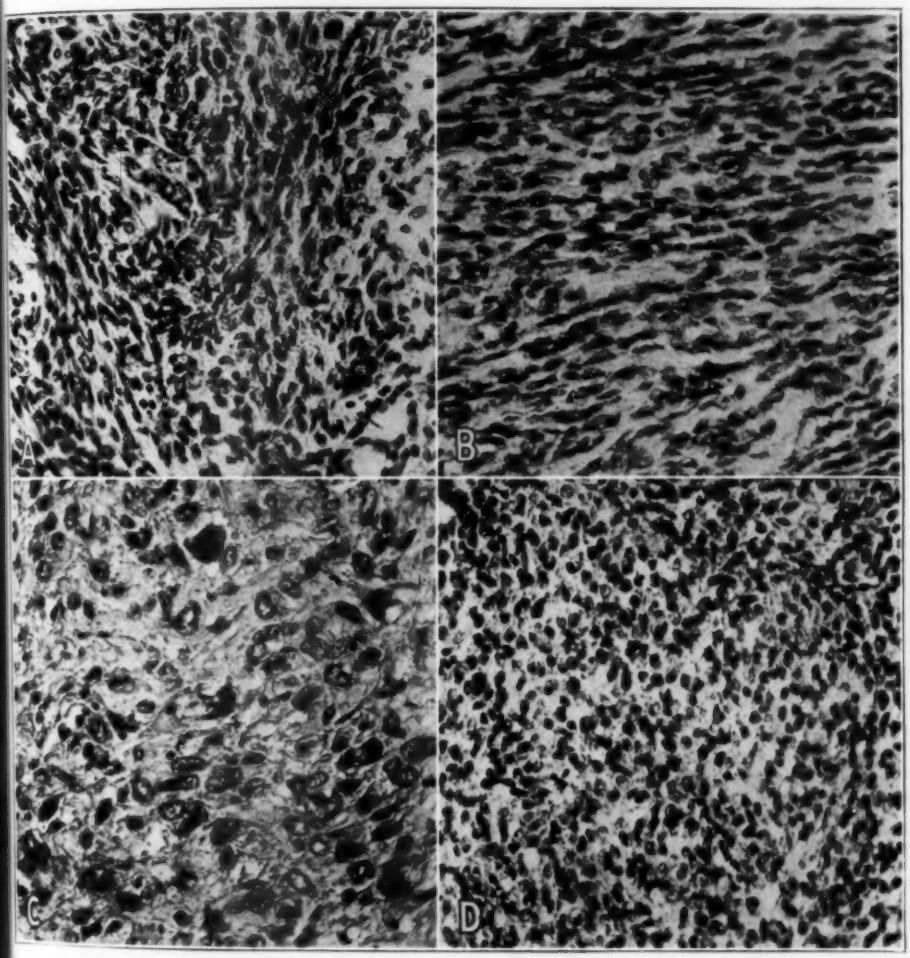

Fig. 4.—High power photomicrographs (same degree of magnification), showing the four grades of malignancy observed in cases of periosteal fibrosarcoma. *A*, grade 1; *B*, grade 2; *C*, grade 3; *D*, grade 4.

the same throughout the whole tumor. Figure 4 illustrates the microscopic characteristics of the four grades of malignancy under high power magnification.

In 3 cases in which repeated local excisions were done there was a definite progression in the grade of malignancy. Figure 5 illustrates such a change. This finding tends to support the dictum that with recurrence the tumor frequently becomes more malignant.

TREATMENT AND PROGNOSIS

The age of the patient, the location of the tumor, the extent of the osseous involvement, the presence or absence of metastases on admission and the degree of malignancy noted on microscopic examination were the factors which determined the type of treatment in this series. Table 1 shows the type of treatment employed and the results obtained in the 25 cases in which follw-up studies were made.

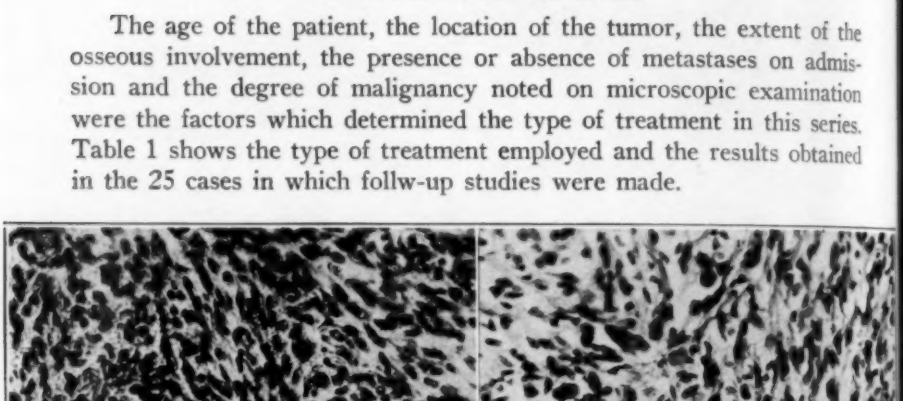

Fig. 5.—High power photomicrographs showing progression in the grade of malignancy from 1 to 3 with repeated local excision in the same patient. *A*, grade 1; *B*, grade 3.

TABLE 1.—*Analysis of Twenty-Five Cases of Periosteal Fibrosarcoma Based on the Type of Treatment*

Treatment	Number of Cases	Location	Mortality, per Cent	Average Survival of Living, Months	Average Survival of Dead, Months	Number of 5 Year Survivals	Percentage of 5 Year Survivals
Symptomatic	1	1 Upper extr.	100	..	2 days	0	0
Roentgen therapy only	3	3 Lower extr.	67	14	12	0	0
Local excision plus roentgen therapy	10	6 Skull 2 Spine 2 Upper extr.	50	93	36	6	60
Amputation	11	4 Upper extr. 7 Lower extr.	45	92	26	4	36
Totals	25	25	52	86	28	10	40

The patient who received symptomatic treatment only was moribund on admission and died within two days.

Three patients received roentgen therapy only. In only 1 case was it the treatment of choice. The patient was a 68 year old woman with hypertension, hypertensive heart disease and a grade 3 periosteal fibrosarcoma of the femur. Fourteen months after treatment this patient reported that the tumor was giving her no trouble and that it was definitely smaller than before treatment. One patient with a tumor of the femur refused any type of treatment after biopsy except roentgen therapy. This patient died seventeen months after treatment. The third patient had far advanced pulmonary metastases on admission and died four months after treatment.

All of the patients with lesions of the spine and of the skull were treated perforce by local excision. One lesion involving the humerus and another involving the ulna were also treated by local excision; both of these lesions were of a low grade of malignancy and showed relatively little involvement of the underlying bone. The patient with the lesion of the ulna is living and well twelve and one-half years after treatment. The patient with the lesion of the humerus had a local recurrence of a higher grade of malignancy, which was treated by repeated local excision; this patient succumbed to metastases to the lungs almost seven years after the first local excision.

Local excision of lesions of the extremities was followed by amputation in 4 cases. In 1 case the amputation followed the local excision after a few days, and the amputated specimen showed no evidence of a malignant lesion. In the other 3 cases amputation was done because of local recurrence. In 7 cases a primary amputation was done at the usual sites of election.

Local excision was followed in almost every instance by roentgen therapy. The value of roentgen therapy for periosteal fibrosarcoma has never been definitely proved. It is generally supposed to be of no value. However, 3 cases deserve special mention. As has been noted, 1 of the patients who received only roentgen therapy reported fourteen months after treatment that the tumor of the thigh was definitely smaller and was causing her no trouble. The second patient had metastases to the lungs two months after a disarticulation of the hip for a lesion of the lower end of the femur. Roentgen therapy to the chest resulted in complete disappearance of the pulmonary lesions, and a check-up examination fourteen months later showed no evidence of their recurrence. The third patient received roentgen therapy to a large tumor arising from the spine, which showed a 75 per cent reduction in size before local excision was carried out.

Follow-up studies were made in 25 cases, or 93 per cent, of this series. At the time of writing, 12 patients, or 48 per cent, were living,

and 13, or 52 per cent, had died. Among the living, the average duration of the disease from the onset until the time of writing was one hundred and two months, and from the time of treatment until the time of writing, eighty-six months. Among those who subsequently died, the average duration of the disease from the onset until death was forty-seven months, and from the time of treatment until death, twenty-five months. Ten patients survived more than five years after treatment, an incidence of 40 per cent. The fact that 3 of these 10 patients died of their malignant lesions more than five years after the institution of treatment is another demonstration of the absurdity of the designation "five year cures."

The patients who died succumbed for the most part to metastases, which were almost invariably to the lungs. Five patients had metastases on admission, 4 to the lungs and 1 to the regional lymph nodes and later to the lungs. Of the remaining 8 patients, 4 had metastases

TABLE 2.—*Analysis of Twenty-Five Cases of Periosteal Fibrosarcoma Based on the Location of the Lesions*

Location	Number of Cases	Mortality, per Cent	Number of 5 Year Survivals	Percentage of 5 Year Survivals
Spine	2	100	0	0
Skull	6	33	5	83
Upper extremity	7	71	3	43
Lower extremity	10	40 (60%)	3	30

to the lungs subsequent to treatment, while in the cases of the other 4 the precise mode of death was not established.

To determine the prognosis of periosteal fibrosarcoma an attempt was made to evaluate the following factors: the duration of symptoms prior to admission and treatment, the location of the lesion, the type of treatment and the grade of malignancy. Among the patients who were living at the time of writing, 80 per cent had had symptoms for six months or less from the onset until admission to the hospital. Among those who died, 75 per cent had had symptoms for a year or more prior to admission. This supports the rather obvious contention that treatment, to be effective, must be started early in the course of the disease.

An analysis of the end results based on the location of the tumor furnished the results shown in table 2. The lesions affecting the spine were relatively inaccessible, and no more than a partial excision could be done. The lesions affecting the skull were more accessible, and in spite of the fact that local excision was carried out in each case, accompanied with roentgen therapy, the results of treatment were excellent. On the other hand, the lesions of the extremities, which were treated in the majority of cases by amputation, were associated with a much higher mortality and a much smaller percentage of five-year survivals.

The results with lesions of the lower extremity were really less favorable than is indicated, because 2 of the patients who were living had metastases to the lungs. It is evident that, with the exception of the lesions in the spine, the location of the tumor was probably not the determining factor in the outcome of the disease.

It will be noted from table 1 that the mortality among those patients who had a local excision plus roentgen therapy was approximately the same as among those who underwent amputation, while the percentage of five year survivals was much higher among those who were treated by the less radical procedure. It seems justifiable to conclude that the particular type of treatment employed was not the most important factor in determining the outcome of the disease, since amputation should result in a more favorable prognosis for life.

TABLE 3.—*Analysis of Twenty-One Cases of Periosteal Fibrosarcoma Based on the Grade of Malignancy*

Grade of Malignancy	Number of Cases	Mortality, per Cent	Average Survival of Living, Months		Average Survival of Dead, Months		Metastasis		Number of 5 Year Survivals	Percentage of 5 Year Survivals
			After Onset	After Treatment	After Onset	After Treatment	On Admission	After Treatment		
1	2	50	106	100	67+	67	0	0	2	100
2	10	20	120	85	65	48	0	1	7	70
3	8	63	22	14	27	11	3	3	0	0
4	1	100	..	..	6	3	0	1	0	0

Table 3 offers a striking indication of the influence of the grade of malignancy of the tumor on the prognosis. The mortality was much greater for the higher grades of malignancy. The 63 per cent mortality for grade 3 will undoubtedly increase to 88 per cent, because 2 of the 3 living patients had pulmonary metastases. The average survival periods for the living and the dead were in inverse proportion to the grade of malignancy. Of the patients who had known metastases, all but 1 had lesions of grades 3 and 4. All of the patients who survived for as long as five years had lesions of grades 1 and 2. It should be noted that the grades of malignancy were determined without reference to any but the microscopic features of these tumors.

The implications of the grade of malignancy for treatment are that more conservative measures, such as local excision, with or without roentgen therapy, may be attempted with grades 1 and 2; tumors of the higher grades of malignancy should be treated by more radical means, namely, amputation when possible and the widest possible local excision in locations in which amputation is impossible. The determination of the grade of malignancy is made from fixed microscopic sections; hence a few days must elapse between the taking of a biopsy specimen and the final treatment. In those cases in which the decision

between local excision and amputation rests on the grade of malignancy it is considered permissible to wait a few days, as the danger of a short delay between the removal of a specimen for biopsy and the curative operation has never been established.

SUMMARY AND CONCLUSIONS

Periosteal fibrosarcoma is an extremely rare lesion, in this series constituting 1 of every 8 primary malignant tumors of bone. Approximately 75 per cent of the lesions occurred in patients under 40 years of age, the greatest incidence being in young adult life. The sex incidence was almost 2 to 1 in favor of males. The family history was not significant, nor did trauma play an important role. The average duration of symptoms before the diagnosis was established was twenty months. The outstanding symptoms were pain and swelling. The chief physical finding was a firm, deep-seated, smooth tumor without fixation to the overlying tissues but with deep attachment to the periosteum. The lesions were single and occurred most frequently in the extremities, although approximately 25 per cent occurred in the skull. The roentgen characteristics were those of a large soft tissue tumor with either lytic or reactive changes in the underlying bone, the destructive changes being more common. At operation the lesion was found to be firm, generally encapsulated and white and glistening on cut section, with occasional hemorrhagic changes. There was usually destruction of the underlying bone. The microscopic features were essentially the same as those of any sarcoma of fibrous tissue origin.

The treatment consisted, usually of either local excision or amputation. Roentgen therapy was the usual adjunct to local excision and for inoperable lesions was used as a palliative measure. The choice of treatment depended on the age of the patient, the location of the tumor, the extent of the osseous involvement, the presence or absence of distant metastases and the degree of malignancy noted on microscopic examination. The mortality was approximately 50 per cent, and the incidence of five year survivals was 40 per cent. Death was usually due to pulmonary metastases. The grade of malignancy, as noted on microscopic examination, was the most important feature in determining the prognosis. All of the patients who survived for five years or more had lesions of a low degree of malignancy.

A CASE OF INGUINAL ENDOMETRIOMA

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AND

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Since Cullen first described inguinal endometrioma, there have been several cases reported in the literature. This lesion is of general surgical interest, for the preoperative diagnosis has usually been incarcerated inguinal hernia, whether or not a hernia sac was actually present. The aspect of the subject which has gained most attention, however, is the search for an explanation of the pathogenesis.

Sampson mentioned five possible theories which could account for the presence of endometrium in the region of the external inguinal ring: 1. Muellerian tissue might be placed beside the round ligament as a result of faulty embryonic development. 2. Mesothelium in the region of the round ligament might undergo metaplasia. 3. Pelvic endometriosis could reach the groin by direct growth extension. 4. Endometrial metastasis could take place by way of the blood or lymph vessels. 5. If a hernia sac were present, an endometrial implant could reach the groin by way of the peritoneal cavity.

Sampson observed 2 cases of inguinal endometrioma in which there were associated hernias. In 1 instance endometrial implants were found in the wall of an inguinal hernia sac. In the other case a femoral hernia was present on the same side, but the endometrioma appeared to be free of the hernia sac. Christopher reported 1 case and Hilgenfeldt 2 in which endometrial implants were found in inguinal hernia sacs. Polster observed 2 cases of endometrioma attached to the round ligament outside the external inguinal ring in which there was inguinal hernia of the same side, without, however, evidence of serosal implantation. Knoflach reported a similar case.

Sampson presented 1 case of endometrioma of the groin in which endometrial tissue appeared to have reached the inguinal region by direct growth extension through the inguinal canal. The patient had extensive pelvic endometriosis, with implants against the internal inguinal ring. Continuity was apparent between the pelvic endometriosis and the mass in the groin. Kaulich and Gomori reported a case in which

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they observed histologic evidence of endometrial growth along the round ligament.

Cases of inguinal endometrioma have been reported by Cullen, Beck, Blumer, Henry, Meigs and Schmitz in which there was neither a hernia sac nor evidence of endometrial growth extension through the inguinal canal. To explain the presence of endometrial tissue in the groin in

Inguinal endometrioma.

these patients one can refer to the other three possibilities mentioned by Sampson: the congenital rest theory, metaplasia and metastasis. Convincing evidence in favor of any of these theories is lacking.

REPORT OF A CASE

Our patient was a married woman 28 years of age. She was first seen in February 1938. Aside from an attack of colitis that persisted in 1936 and 1937 she had always been well. She had had no pregnancies and no menstrual irregu-

larities or complaints. She complained of pain and of swelling of one month's duration in the right groin. The pain was dull and was more severe at the onset of the menses. She felt that the swelling was about the size of an egg. Coughing, laughing or touching the mass produced pain. Examination showed her to be well developed and well nourished, weighing 130 pounds (59 Kg.). The only abnormal finding was a right inguinal hernia. This was operated on in February 1938, and a sac the size of a lemon was found. Digital examination of the pelvis revealed no pathologic condition. Recovery was uneventful.

Two years later, in January 1940, the patient returned, stating that she had enjoyed good health since the hernia repair but that she had always had some pain in the right groin, that a small lump was palpable and that at her menstrual time there was more pain and the lump increased in size. Examination revealed a mass about the size of a peanut kernel just to the right of the pubes. It was slightly tender when pressed against the pubic ramus. The patient stated that it was definitely larger, and extremely painful, during menstruation.

With the patient under a general anesthesia, an incision was made over the right pubic spine, and the dissection was carried down to a small mass the size of an olive which was in the region of the external ring. The tissues as encountered were adherent in scar as a result of the previous hernia repair. To facilitate dissection the incision was extended obliquely upward, and the course of the round ligament was followed. A part of the round ligament and the tissue mass were then excised. Twice during the procedure small quantities of chocolate-colored fluid were encountered, suggesting the possibility that this tissue was an endometrial implant. The deeper structures were then closed with catgut and the skin with silk.

Pathologic Report.—The specimen consisted of a piece of fibroblastic tissue with some fat attached, which measured 3 by 2 cm. The tissue was firm and fibrous in places, and there no distinct tumor masses were seen. On section through the tissue, the cut surface showed some brown hemorrhagic discoloration. Sections were taken for microscopic study.

Under the microscope the section was seen to consist for the most part of fibrous and fatty tissue. In places there were elongated and dilated acini lined by columnar epithelium and surrounded in part by tissue resembling endometrial stroma.

The diagnosis was endometrioma.

The patient made a good recovery from the operation and has had no complaints since.

COMMENT

This case appears to be similar to those reported by Sampson, Polster and Knoflach, in which endometrioma of the round ligament was associated with the presence of a hernia sac, without, however, evidence of serosal implantation. The possibility exists, of course, that an endometrioma within a hernia sac might afix itself to the round ligament and then undergo partial atrophy, thus leaving the hernia sac free. On the other hand, several cases of endometrioma of the round ligament have been reported in which there was no associated hernia, and the presence of these two lesions in the same patient may have been mere coincidence.

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TIMING OPERATIVE INTERVENTION FOR ACUTE INTESTINAL OBSTRUCTION

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The rather voluminous literature on intestinal obstruction has in recent years undergone a great change. Only a few years ago, Fred T. Murphy said in Ochsner's "Surgical Diagnosis and Treatment:" [1] "For a mechanical obstruction of the bowel, there is no other logical treatment than operation for the relief of the obstruction." The recent literature, however, has shown what a great mistake this was and attests the splendid results obtained by the use of peroral suction of the upper portion of the intestinal tract. The teachings of Wangensteen,[2] Johnston [3] and many others are now so well established and have been confirmed in so many clinics that one must accept them; they require no further proof. Nevertheless, in almost every article dealing with the "conservative" treatment of intestinal obstructions one finds the statement that this is not to be used as a complete substitute for the operative treatment. Wangensteen [4] wrote: "Operation still is, and probably will continue to be the chief mainstay of therapy in most forms of bowel obstruction." This thought is echoed by most of the writers who extol the values of conservative methods. It is, however, difficult to determine in which cases operation should be done immediately and in which cases conservative methods should be attempted and when they should be abandoned for operative intervention. In an attempt to clarify this issue, the following study was undertaken.

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2. Wangensteen, O. H.; Rea, C. E.; Smith, B. A., Jr., and Schwyzer, H. C.: Experiences with the Employment of Suction in the Treatment of Acute Intestinal Obstruction, Surg., Gynec. & Obst. **68**:851 (May) 1939.

3. Johnston, C. G.; Penberty, G. C.; Noer, R. J., and Kenning, J. C.: Decompression of the Small Intestine in the Treatment of Intestinal Obstruction, J. A. M. A. **111**:1365 (Oct. 8) 1938.

4. Wangensteen, O. H.: The Therapeutic Problem in Bowel Obstruction, Springfield, Ill., Charles C. Thomas, Publisher, 1937.

We first tried to classify the types of intestinal obstruction from the therapeutic standpoint and then attempted to find certain clinical signs which would permit such a clinical grouping (table 1). These signs were gleaned from a review of a series of case records in the files of the Cook County Hospital. We have not discovered any new signs, nor have we in this review contributed any new methods; rather, we are attempting to present a working plan for integrating the individual case of intestinal obstruction into the therapeutic plan and to present a few examples which demonstrate the workability of this procedure.

As will be observed from table 1, we classify intestinal obstructions into: (1) those urgently demanding operative intervention; (2) those to be treated conservatively for an arbitrary period, and (3) those to be managed entirely by conservative methods or operated on at a time of election. That is, we determine whether by the symptom complex the condition fits into the first group; if it does not, it falls automatically into the group for which delayed treatment is permissible. At any time during

TABLE 1.—*Classification of Therapy for Acute Obstruction of the Bowel* *

1. Immediate Operation	2. Delayed Operation	3. Conservative Treatment
Complete colonic obstruction	Internal hernias	Bands and adhesions
Strangulation obstruction	Obturation by foreign body	
Intussusception	Internal pseudohernia	
Intestinal atresias		

* This classification is by no means hard and fast as strangulation may develop in the patient who has an internal hernia or even an adhesion band, thus classifying the condition in group 1.

the period of expectant therapy the patient may present additional signs which automatically advance his condition into the urgent group. At the end of the arbitrary time, which we have set at forty-eight hours, the clinical status is reviewed to determine whether the condition now belongs in the "delayed" group or passes on into the "conservative therapy" group. We cannot, however, emphasize too strongly that at any time in the course of conservative therapy there may be urgent indications for intervention. This necessitates constant observation, and the surgeon cannot relax his vigilance in the feeling of false security that is often engendered by the use of the suction catheter and intravenous fluids.

In this discussion we shall make no mention of external hernias, although they are a major etiologic factor in intestinal obstruction. Their diagnosis should not be fraught with difficulty in most instances, and their care forms a separate chapter of surgical therapeusis. Reference will later be made, however, to two important complications of the manipulative reduction of external hernia, namely, reduction of gangrenous bowel and reduction en masse.

CONDITIONS URGENTLY REQUIRING OPERATIVE INTERVENTION

1. *Complete Obstruction of the Colon.*—Complete colonic obstructions must be, as Wangensteen [4] has pointed out, considered as closed loop obstructions. This is true because of the invariable competence of the ileocecal valve in the presence of obstruction of the colon. Therefore, if the obstruction is truly complete, tremendous distention will usually take place. This cannot be relieved by vomiting, nor will the Levine catheter and suction be of any avail. We have not observed any reports of a Miller-Abbott tube being passed through the ileocecal valve in the face of a colonic obstruction, although this is not inconceivable. Most colonic obstructions are not truly complete. In the majority of cases (86.7 per cent in Burgess' [5] series) the obstructing lesion is an annular carcinoma of the left side of the colon, the lumen of which has become obturated by fecal material, often of vegetable origin. This obturation often can be washed free by enemas, which transforms the complete obstruction into a chronic or partial obstruction, and can then be treated accordingly.

The diagnosis of colonic obstruction is based on the following clinical picture. The patient is usually of middle age or advanced years and has often been a sufferer from constipation and abdominal discomfort for some time. Often there is a history of successive attacks of partial obstruction, which have been relieved by catharsis or by enemas. In many instances a history of blood and mucus in the stool or of diarrhea is obtainable. Vomiting is usually very slight, considering the degree of distention. The patient frequently does not look as ill as the findings would suggest. On physical examination the abdomen is found to be distended and smooth. The distention goes well out into the flanks, while the umbilicus may not be very much raised above the xiphopubic level. The abdomen is soft, and tenderness, if present, is in the cecal area. Rushes of peristalsis will be heard in practically all cases, but, as Vaughan and Thorek [6] have pointed out, the interval between the rushes may be considerable, necessitating auscultation for five minutes or more. Digital rectal examination may reveal the neoplasm in the rectum, although carcinoma of the rectal ampulla does not as a rule produce acute obstruction. Tympany will extend into the lumbar region, and scratch sounds may also be heard well into the lumbar area. Dulness of the liver is usually reduced and may be absent.

The diagnosis can usually be confirmed by the use of a 2 quart (1.8 liter) tap water enema. The normal colon will accommodate itself to this amount, but a patient with an obstructive lesion of the left side of

5. Burgess, A. H.: Discussion of the Treatment of Obstructions of the Colon, Brit. M. J. **2**:547 (Sept. 29) 1923.

6. Vaughan, R., and Thorek, P.: Abdominal Auscultation, Am. J. Surg. **45**: 230-234 (Aug.) 1939.

the colon will usually permit only a fraction of this amount of water to be given, on account of pain incident to distention by the enema. Some surgeons are reluctant to make use of the tap water enema, fearing a perforation. This is not to be feared with the obstructive lesions as a rule, because the point of perforation (and thus the point of weakness) is either the cecum (Wangensteen [4]) or the point of the stercoral ulceration just above the obstructing lesion. The enema, however, in the presence of complete colonic obstruction does not pass the carcinoma and is, therefore, innocuous. The diagnosis is furthered by the flat plate of the abdomen. It is true that in rare cases a small amount of gas will be observed in the terminal portion of the ileum, but usually the gas pattern is entirely colonic.

This can be differentiated in the manner suggested in table 2. Wangensteen depreciated the information given by the barium sulfate enema. We have, however, found it valuable in several cases, especially

TABLE 2.—*Roentgen Signs of Obstruction of the Small and of the Large Bowel*

Small Intestine	Large Intestine
Paralleling of loops	Inverted horseshoe configuration
Valvulae conniventes *	Haustral markings *
Stepladder fluid levels	Large fluid levels

* The valvulae conniventes are seen as small indentations in the gas pattern. If one carefully observes the outside of the bowel wall, which will appear as a gray shadow, one can see that it describes a straight line (fig. 2). This is caused by the valvulae, which are folds of mucous membrane. In contrast, the haustral markings will be observed as much larger indentations which are from the outside of the colon (fig. 3). The haustra are caused by the shortening of the colon by the inflexible length of the taenia coli.

those in which it is difficult to establish the diagnosis of small or large intestine in the flat plate of the abdomen.

It will be noted that the administration of the tap water enema is both a diagnostic and a therapeutic procedure, for it will often transform an apparently complete colonic obstruction into a chronic one. We should also like to emphasize that tap water, not soapsuds, is used. The latter type of clysis is irritating, and a spastic type of obstruction will react badly. Also, the irritating substance makes it difficult to use the entire 2 quarts even in a normal colon, which will easily accept a similar amount of warm tap water. The only contraindication to the use of such enemas is the suspected presence of a perforation. As we have pointed out in a previous report,[7] this is to be suspected in the presence of signs of peritonitis.

2. *Strangulation Obstruction.*—There is but little argument that strangulated loop obstruction must be subjected to emergency operative intervention. The only time to be expended in preparation is that

7. Koucky, J., and Beck, W. C.: Acute Nonmalignant Perforations of the Colon, Surgery **7**:674, 1940.

required to replenish the loss of blood. The diagnosis of a strangulated loop is made on the diagnosis of an intestinal obstruction (intestinal colic with vomiting and/or distention and/or obstipation) combined with the signs of peritonitis. It is probable that there are only very rare cases in which the arterial blood is completely shut off in the presence of strangulation. In nearly all instances the venous circulation is disturbed and there is a tremendous passive congestion, which soon gives way to hemorrhage, first into the tissues of the intestine and then into the lumen of the intestine and into the free peritoneal cavity. This initiates aseptic peritonitis. The cardinal signs of peritonitis are tenderness, rebound tenderness and paralysis of the intestines, that is, a silent abdomen. We have observed tenderness and rebound tenderness in a few cases of simple obstruction even before the peritoneum was grossly contaminated. In a series of 35 cases of strangulated loop intestinal

TABLE 3.—*Symptoms and Signs of Strangulated Loop Obstruction (35 Cases)*

History of cramping pain	35	
History of borborygmi audible to patient	10 *	
Vomiting	33	
Obstipation	32	
Distention	27	
Tenderness	32 †	
Rebound tenderness	30 †	
Fever (rectal temperature above 99 F.)	27	
Leukocytosis	24	
Increased sediment rate	6	(of 10 studied)
Silent abdomen	35	

* Probably an incomplete statistic, as this is not often asked for or volunteered.
† Response in other cases definitely noted as negative.

obstruction (table 3) there were 5 cases in which rebound tenderness was entirely absent and 3 cases in which no tenderness was exhibited. In all of the 35 cases, however, the abdomen was silent to five minute auscultation. The systemic reaction varied, 27 of the 35 patients having a febrile reaction and 24 having polymorphonuclear leukocytosis. The sedimentation rate of the red blood cells we have found to be a completely unreliable guide.

As these patients in most instances entered the hospital after the strangulation was already in existence, they presented the signs of peritonitis with paralytic ileus. We have found this a most difficult condition to differentiate (case 1). The history may be significant. The patient may state that at the onset of the disease there were intermittent cramping pains associated with rumbling sounds in the abdomen. These sounds may have been audible to the patient or to a relative at the onset of the disease. A patient with acute appendicitis will often have cramping pains at the onset, but these are rarely associated with borborygmic sounds. The most valuable aid to the diagnosis will be the flat plate of the abdomen, for in cases of strangulation of the small

bowel, only the small intestine will appear distended (fig. 1), while in cases of bacterial peritonitis both the small and the large bowel (fig. 2) will be distended (table 2). In the case of a volvulus, only a huge distended loop will be seen, which resembles neither small nor large intestine.

Under the heading of strangulated loop obstruction belong two other lesions which from their physical and roentgen signs are indistinguish-

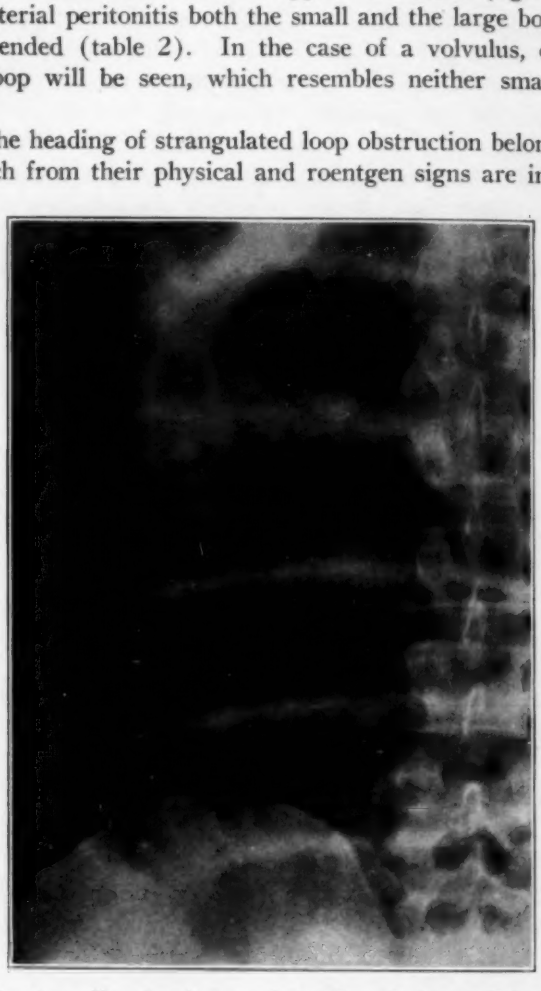

Fig. 1.—Roentgen film showing an obstruction of the small bowel. Note the paralleling of the loops. Note the absence of gas in the large bowel in the flank. The film was taken with the patient in the horizontal position.

able from volvulus. They are venous mesenteric thrombosis and reduced strangulated hernia. The former may be slow in onset or may follow a fulminating course. The lesion occurs primarily in patients with diseased hearts and is well nigh hopeless. The diagnosis of a reduced strangulated hernia, when it has been reduced by the surgeon, is self evident. Cases of spontaneous reduction in the presence of strangulation are recorded but are too rare to be considered. The patients present the classic signs of mechanical obstruction plus those of peritonitis.

3. *Irreducible Intussusception.*—This condition is a variety of strangulation obstruction, but the strangulated loop in this instance is encased in normal intestine. Thus the hemorrhage does not reach the free peritoneal cavity but is passed into the fecal current and is observed in the stool. It is not in the province of this paper to discuss the diagnosis of intussusception, as it has been adequately reviewed in nearly all surgical textbooks.

Fig. 2.—Detail film showing the pattern of an obstruction of the small bowel. Note the valvulae conniventes and the outside of the bowel, which does not assume the configuration of the valvulae but rather assumes a straight line. This has been demonstrated by a line drawn on the picture.

4. *Conditions Eventually Surgical.*—Wangensteen has pointed out that nothing is gained by delaying operation for atresias of the intestinal tract, including imperforate anus, and these should therefore be subjected to operative intervention as early as the diagnosis has become established.

CONDITIONS AMENABLE TO DELAYED OPERATIVE INTERVENTION

Into this group fall those conditions associated with symptoms and signs which do not place them in the urgent group. As has already been stressed, the patients may become imperatively in need of operation, and the signs of peritonitis, namely, tenderness, rebound tenderness and disappearance of the intestinal sounds, must be constantly looked for. During the period of conservative therapy, the treatment is

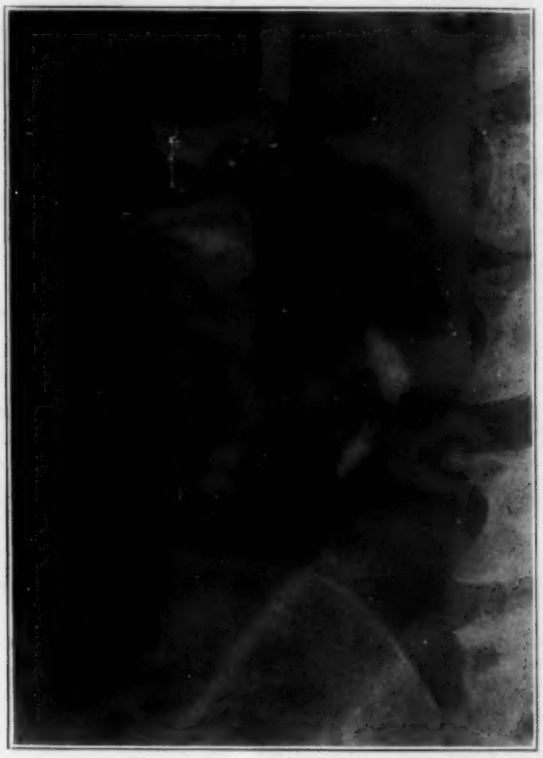

Fig. 3.—Detail film showing the pattern of a haustrum in a case of obstruction of the large bowel. Note that the outside of the intestinal wall follows the haustral contour and is indented. This has been demonstrated by lines drawn on the picture.

essentially as has been outlined by the many authors in this field.[8] We add to the usual therapy the parenteral administration of vitamin K. At four hour intervals the patient's tube is clamped off for one-half hour; 2 ounces (60 cc.) of liquid petrolatum is injected through the tube (as suggested by Vaughan), and the patient is given a tap water enema.

8. Wangensteen and others.[2] Johnston and others.[3]

These enemas are discontinued if they cause the patient much discomfort. The amount of distention as related to the contour of the abdomen and to the xiphopubic line is noted. Another flat plate of the abdomen is made in forty-eight hours, and at this time the clinical status of the patient is reviewed. The signs of systemic reaction, the pulse rate, the temperature and the leukocyte count are checked. If the patient is beginning to show signs of toxicity, operation is believed to be indicated. If the dis-

Fig. 4.—Roentgen film showing a volvulus of the sigmoid flexure. Note the huge gas pattern of double contour having its apex in the left upper quadrant but its root in the left lower quadrant. No other lesion presents a similar picture.

tention has not improved, as observed by the abdominal contour or by the amount of gas seen in the flat plate of the abdomen, operative intervention is believed to be indicated. Also, if the intestinal tract, as evidenced by the recovery of oil administered through the tube and obtained by the enema, is not yet open, we believe that the patient should be subjected to operation.

In this group we have found that the cause of the obstruction is usually obturation by a gallstone or a foreign body, an internal hernia or

a loop of intestine which has slipped under an adhesive band, forming a sort of pseudohernia (case 3). Also in this group will fall the condition seen in patients on whom reduction en masse has been performed after an attempt at manual reduction of external hernias.

CONDITIONS AMENABLE TO CONSERVATIVE THERAPY

Into this group will fall all of the conditions which show some response to the conservative method during the first forty-eight hours. It will be found that this is the largest group and that most patients with intestinal obstruction will have a recovery of oil in the enemas within this time. Into this group will fall nearly all of the postoperative intestinal obstructions and those due to kinks and bands. In a small percentage of the cases, however, the obstruction will recur as soon as the suction is discontinued, even if this is maintained for a long period. Operation is best performed at a time of election, that is, when the fluid, electrolyte, protein and vitamin balance has been adequately controlled.

REPORTS OF ILLUSTRATIVE CASES

CASE 1.—A Negro aged 32 years entered the Cook County Hospital in February 1940. He had been under treatment previously for several months for polyposis of the colon. On the afternoon of admission he underwent fulguration of a polyp in the upper part of the rectum. About six hours after this treatment, there suddenly developed acute abdominal pain.

The physical findings at this time were those associated with perforation of the colon. Recovery was secured by exteriorizing the perforated segment. About four weeks after the operation the patient again suddenly had severe pains in the abdomen. This abdominal pain was mostly in the epigastrium and was cramping. With each of these abdominal cramps peristalsis was audible all over the room. The abdomen was flat, but within an hour it seemed slightly distended. The patient did not pass any gas through his colostomy opening, but an enema administered through this opening went in with ease, and the patient retained approximately 1,000 cc. Auscultation of the abdomen revealed definite rushes of high-pitched tinkling sounds. A flat plate of the abdomen revealed distention of the small intestine in the upper right portion of the abdomen. Approximately four hours later, in spite of Wangensteen suction and intravenous fluids, the patient appeared worse. Auscultation of the abdomen at this time revealed a complete absence of intestinal sounds. At this time the abdomen was also becoming tender and showed evidence of rebound tenderness. The patient was, therefore, prepared for emergency operative intervention, with a diagnosis of a strangulated loop of intestine, which probably had slipped alongside the colostomy.

At the operation the peritoneal cavity was filled with blood-stained fluid. A loop of about 5 feet (160 cm.) of strangulated intestine (not gangrenous) was found and eviscerated. It was found that this loop of intestine had become twisted and at the apex of the volvulus was Meckel's diverticulum, which contained a penetrating ulcer at its apex. This penetrating ulcer had become adherent to the anterior abdominal wall and thus formed an anchor point for the volvulus. The loop was untwisted, the diverticulum resected and the abdomen closed. The patient made an uneventful recovery.

Comment.—This case was interesting because we were able to observe the development of the signs of peritonitis from their inception. At first we had only the evidence of an intestinal obstruction without the manifestation of peritonitis. After four hours, however, the abdomen exhibited tenderness and rebound tenderness and became completely silent. Had we seen this patient later, after the peritonitic signs had developed, it would have been possible to differentiate the strangulated

Fig. 5 (case 1).—Roentgen film of a volvulus of the small bowel. Note the two opposed loops of gas-distended intestine. In this case there was pseudoknotting in which two loops were strangulated. The gas in the upper part of the film is judged to be in the stomach.

loop from peritonitic ileus only by the roentgenogram, which was typical (see report of case 5).

Case 2.—A 65 year old white man entered the Cook County Hospital in January 1940. He stated that he had been perfectly well until six months before admission, at which time he noticed that he was becoming increasingly more constipated. He found that he had to take liquid petrolatum and then magnesium hydroxide almost daily in order to keep his bowels open. Five days before

admission he noticed cramping pains in the abdomen, which he attributed to gas. These cramping pains were often associated with loud gurgles which he could definitely hear. On the first day of this period he passed small amounts of gas, but after this he had been unable to have any bowel movement or to pass any gas. He also noted that his abdomen became more and more distended. He lost his appetite and on one occasion vomited, although only a very small amount. There had been no previous surgical intervention and no previous illnesses that he remembered.

On physical examination he was found to be rather emaciated. He looked older than the age given. Examination of the chest revealed a somewhat enlarged heart and muffled heart tones. Examination of the abdomen showed it to be grossly distended, the distention going well out into the flanks. He had a small direct inguinal hernia, which was easily reducible. No femoral hernias were evident. Percussion of the abdomen revealed it to be tympanitic throughout, with a marked reduction of hepatic dulness. Palpation did not reveal any tumor masses or areas of tenderness or rigidity. On auscultation there were high-pitched borborygmic sounds, which came in rushes and were separated by long silent periods. Rectal examination gave entirely negative results except for a slightly enlarged prostate gland. The temperature, pulse rate and leukocyte count were within normal limits, and there was moderate secondary anemia. A flat plate was taken of the abdomen, which revealed a typical colonic pattern and a colonic type of distention. A barium sulfate enema was administered, but the barium did not pass beyond the rectosigmoid juncture. An attempt was made to give a 2 quart (1.8 liter) enema, but the patient was able to take only about a pint (0.9 liter). About an hour later a second 2 quart enema was administered, and at this time there was a sudden rush of sound as the enema passed the obstructed point. After administration of the enema, of which the patient took approximately a quart, there occurred the passage of a large amount of gas, and this was followed by the passage of fecal matter. The abdominal distention rapidly disappeared. The patient was given 2 ounces (60 cc.) of liquid petrolatum by mouth and a 2 quart enema every four hours. Twenty-four hours later he appeared to be clinically well. After another twenty-four hours a barium sulfate enema was again administered, and this revealed a carcinoma of the rectosigmoid junction, which was removed after proper preoperative care.

Comment.—This represents the most common type of obstruction of the large bowel, in which there is a narrowing of the lumen by carcinoma of the rectosigmoid juncture. The narrow lumen is then obturated by fecal matter. This at times can be washed away by an enema, which transforms a complete colonic obstruction into a partial or chronic colonic obstruction.

Case 3.—A white man aged 66 years entered the Cook County Hospital in February 1940. He stated that he had been perfectly well except for slight constipation until one week before admission. At this time he had considerable difficulty in having a bowel movement and gave himself several enemas, which were successful. Four days before admission he noticed cramping pains in the abdomen. These cramps came at three to four minute intervals; they were severe, and he attempted to pass gas but was unable to do so. He noticed no gurgles or other sounds. He tried to give himself enemas but was unable to do so and took castor oil, which did not come out but produced severe abdominal cramps. These were followed by considerable vomiting. His abdomen became more and more distended.

For four days before admission he had not passed any gas, nor had he had a bowel movement. He admitted losing considerable weight in the last year but did not know how much.

Physical examination gave entirely negative results for a moderate amount of emaciation. The abdomen was grossly distended to about 4 fingerbreadths above the xiphopubic line; the distention appeared to be still greater in the flank. There was a scar of an old herniorraphy on the left side. The percussion note was tympanitic throughout, and the hepatic dulness was obliterated. On auscultation

Fig. 6 (case 3).—Roentgen film of a complete colonic obstruction. Note that the pattern of gas follows the general pattern of the distribution of the colon. The patient had a carcinoma of the rectosigmoid juncture.

rushes of peristalsis with interspersed silent periods were easily audible. Rectal examination gave entirely negative results. A flat plate of the abdomen showed a typical colonic distribution of gas with great dilatation of the intestinal loops. An attempt was made to administer a barium sulfate enema, but the patient could not retain any of the barium. A quart (1.8 liter) tap water enema was tried, but the patient took less than a pint. He was given 2 ounces (60 cc.) of liquid petrolatum, and two hours later a second and a third attempt were made to give a 2 quart enema, but both were unsuccessful. The patient vomited several times during the intervening period. It was decided that this patient had a complete

colonic obstruction and that, therefore, emergency intervention was indicated. With local anesthesia, a typical McNealy cecostomy was performed.[9] It was noted that there was an enormous distended cecum, while the terminal portion of the ileum appeared to be completely collapsed. The cecostomy wound was opened twenty-four hours later and drained a large amount of gas. Forty-eight hours later the patient had a small bowel movement by rectum. He made an uneventful recovery, and approximately three weeks later the cecostomy closed.

Comment.—This is the type of condition which is referred to in the foregoing sections as complete obstruction of the colon. It presents an indication for emergency surgical treatment. It has been our experience that frequently a cecostomy is done for such a condition and the patient has a normal bowel movement a short time thereafter. This does not mean that the cecostomy has been performed in vain. Probably some of the edema around the tumor has been diminished with the relief of the pressure. The cecostomy stoma closes spontaneously, and we believe that the operation is in these cases a life-saving procedure.

Case 4.—A white woman aged 64 was admitted to the Cook County Hospital in June 1939, complaining of cramping abdominal pains, vomiting, distention and complete obstipation for two days. She had always been perfectly well until the onset of the aforementioned symptoms. On further questioning she told us that she had heard loud rumbling sounds in the abdomen with each of these pains. On physical examination she did not appear acutely ill. The temperature was 99.6 F.; the pulse and respiratory rates were normal. The white blood cell count was 9,400 per cubic millimeter. Examination revealed muffled heart sounds and considerable cardiac enlargement. The abdomen was distended to approximately 5 cm. above the xiphopubic line. There was no tenderness or rebound tenderness at any point in the abdomen. It was tympanitic throughout, and the hepatic dulness was much diminished. Vaginal and rectal examinations did not reveal any significant findings. Auscultation of the abdomen showed rushes of high-pitched, obstructive peristaltic sounds at intervals of about one minute.

A flat plate of the abdomen revealed a typical distention of the small bowel. A diagnosis was made of obstruction in the small intestine without any evidences of strangulation. The cause was somewhat obscure, as there were no scars of previous operations on the abdomen. The patient was therefore treated conservatively. A Levine tube was introduced and connected with a Wangensteen type of suction apparatus, and intravenous fluid was administered. At the end of forty-eight hours the patient appeared considerably brighter. There were no evidences of dehydration or of strangulation. The peristaltic sounds were somewhat quieter but were still coming in rushes. The abdominal distention, however, had not abated. A second flat plate of the abdomen at this time did not reveal any reduction in the size of the intestinal loops. It was therefore decided to operate on this patient, as she was in good condition. Operation was done with spinal anesthesia. At the junction of the collapsed and distended loops a large mass was felt in the lumen of the intestine. This mass was presumably a large gallstone. It was pushed upward into the distended loop of intestine, and this permitted gas to pass on to the collapsed portion

9. McNealy, R. W., and Lichtenstein, M.: Simple Technique for Cecostomy, Am. J. Surg. **36**:620-622 (June) 1937.

of the intestine. The mass was then pushed downward into the more normal intestine, and it was found possible to push it approximately 1 inch (2.5 cm.) beyond the point of the original obturation. A longitudinal incision was then made directly above the foreign body, and this body was extruded. It proved to be a large gallstone. The incision in the intestinal wall was closed in a transverse direction. The patient had an uneventful course for six postoperative days and then suddenly had a massive collapse of the lung followed by severe pneumonia, from which she died.

Comment.—The condition of this patient exemplifies those in the delayed group. The fatal outcome does not alter the surgical result but rather demonstrates that certain complications will follow even in patients who, one believes, are properly cared for. The patient had been given adequate preoperative care and was in splendid condition at the time of the intervention. Nevertheless, nothing could be gained by delaying the operation.

CASE 5.—A woman aged 28 was admitted to the Cook County Hospital on Oct. 12, 1939. She stated that she had been operated on three months previously for "acute tubal infection," and that the tubes had been removed. After the operation she had a slow convalescence, and there was a high fever for several weeks. Eventually she was discharged from the hospital but continued to have considerable vaginal discharge. On the day before admission she suddenly had severe abdominal cramps and (on questioning just before operation) admitted that they had been associated with gurgling sounds in the abdomen. She vomited a great deal but had had some passage of flatus and a small bowel movement. On examination the abdomen was found to be slightly distended and very tender, and it showed evidences of rebound tenderness, especially in the left lower portion. The temperature was 100 F. (rectal), and the leukocyte count, 16,000 per cubic millimeter. Vaginal examination revealed so much tenderness that no organs were palpable. The abdomen was entirely silent.

A tentative diagnosis was made of diffuse peritonitis probably originating from a ruptured pelvic abscess. The patient was sent to a medical service. The febrile condition continued and soon assumed a septic aspect. The abdominal distention increased and was not controlled by continuous suction. After three days surgical consultation was sought. The only finding different from those aforementioned was that the abdominal distention was slightly irregular. A flat plate of the abdomen was taken, and this (fig. 5) revealed a single distended loop, suggestive of a volvulus. The patient was operated on immediately with spinal anesthesia. At operation a gangrenous volvulus of 5 feet of jejunum and ileum was found, which had already perforated. The loop was exteriorized. The patient died on the second postoperative day.

Comment.—This case well illustrates the difficulty in differentiating late strangulated loop intestinal obstruction with peritonitis from bacterial peritonitis with secondary paralytic intestinal obstruction. The condition of the patient had been considered as a clear example of the latter type for three days. When she was first seen by one of us it did not appear in any different light, but we ordered a routine flat plate of the abdomen. This demonstrated the lesion immediately, and within one

hour the patient was prepared for operation. Had this routine roentgen film been taken three or even two days sooner this patient might have been saved.

Case 6.—A white man aged 32 years entered the Cook County Hospital in October 1939. He stated that he had always been well until twenty-four hours before admission, at which time he suddenly had cramping abdominal pains occurring diffusely throughout the abdomen. The cramps were severe and caused him to become nauseated, and he vomited four or five times during the twenty-four hours before admission. The pain at no time localized to one area of the abdomen. He had heard no rushes or gurgles in his abdomen. He stated that he had had one small watery bowel movement since the onset of this severe pain. He noticed, however, that his abdomen in the last three or four hours before admission gradually became distended. His past history was entirely irrelevant. On physical examination he appeared acutely ill. The temperature was 101.6 F., the pulse rate 120 and the respiratory rate 126. The white blood cell count was 14,000 per cubic millimeter. The heart and lungs were entirely normal. The abdomen was distended 2 fingerbreadths above the xiphopubic line. It was tympanitic throughout, and there was a reduction in the hepatic dulness. There was absolutely no tenderness or rigidity. There was no rebound tenderness. The Rovsing, obturator and psoas signs were negative. Digital examination of the rectum gave entirely negative results, there being neither tenderness nor palpable masses. Auscultation of the abdomen revealed that it was remarkably silent, with only an occasional tinkle. No rushes were heard. A flat plate of the abdomen was taken and surprisingly showed distention of both the small and the large intestine. A small bubble of gas was visualized in the rectum. Although the roentgenogram was typical of ileus due to bacterial peritonitis or to an extra-abdominal lesion, it was believed more probable that the patient had an intestinal obstruction. In the complete absence of tenderness, rebound tenderness and rigidity, the patient was treated with Wangensteen suction and intravenous salt solution was administered. An attempt was made to pass the Miller-Abbott tube, but it passed the pylorus only with great difficulty. After twenty-four hours the patient appeared somewhat more ill than he had on previous examination. There was still no tenderness or rebound tenderness, but the temperature was now 103 F. and the white blood cell count 18,500 per cubic millimeter.

A second flat plate of the abdomen was taken, and this showed even greater distention than had been observed on previous examination. Both the small and the large intestine appeared to be filled with gas. Abdominal exploration was therefore decided on, and a right median incision was made. When the peritoneum was opened it was found that the cavity was filled with pus. The origin of this pus was a ruptured appendix. The appendix was removed, and it was found that both the large and the small intestine were grossly distended. The patient had a very stormy course; a severe wound infection developed, and an infection occurred in the cul-de-sac. But he eventually recovered.

Comment.—This patient shows the extreme difficulty sometimes encountered in differentiating between an intestinal obstruction and the ileus caused by peritonitis. The roentgenogram was diagnostic but was discounted because of the clinical findings and the complete absence of tenderness and rebound tenderness. We readily admit that this is a great rarity.

GENERAL COMMENT AND SUMMARY

Intestinal obstruction remains a deadly disease in spite of a better understanding of its mechanism and lethal factors. Much of the resultant loss of life is due to lack of consideration of details in diagnosis or to delay. These are probably due chiefly to faults of omission, which can occur when seemingly every possible diagnostic effort has been made. The routine discussed obviates some of the errors of omission. It probably will tend to increase certain mistakes in judgment, as a formulization tends to instil confidence, which is often rudely shaken. Every case of intestinal obstruction remains a diagnostic problem which demands repeated careful examination and the most deliberate and mature consideration. During the last few years tremendous advances have been made in the treatment of intestinal obstruction. They demonstrate, however, the inadequacy of the present diagnostic methods. Fuller appreciation of the value of careful observation and readiness to change methods of treatment should lead to a further reduction in mortality. The uniform routine has its limitations when applied to a disease as varied as intestinal obstruction. We have, however, attempted to present such a routine as a general guide for the evaluation of the individual case. We have also attempted, in this manner, to suggest the necessity of careful history taking, the necessity of careful and repeated physical examination and the extreme necessity of using every method of diagnostic approach in the individual case. Our main contention is that there is no one treatment for intestinal obstruction and that most conservative methods, as well as operative intervention, may have an application in the same case or in different cases. There is a definite time, however, when conservative methods must be forsaken for operative intervention. This time must be determined by all of the diagnostic acumen which the surgeon can muster.

PRIMARY CARCINOMA OF THE GALLBLADDER

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Physicians seldom consider carcinoma of the gallbladder a factor of much significance when advising patients with gallstones regarding their management. Repeated emphasis has made the members of the medical profession aware of the possibility of malignant growth developing in some other sites of the body in connection with certain types of lesions. For example, when the roentgenologist reports an ulceration on the gastric side of the pylorus in a person with ulcer dyspepsia, nearly every physician knows the implications as far as malignant growth is concerned. In contrast to this, persons with gallstones are rarely thought of as having or as likely to have a carcinoma of the gallbladder.

Five cases of primary carcinoma of the gallbladder have been observed in a year and a half, and 4 of these were observed within six months. There was only 1 case in which the presence of a malignant tumor was suspected preoperatively; in the other 4 cases the patients were all considered before operation to have benign disease of the gallbladder. It is undoubtedly true that the number of cases observed by one surgeon in this relatively short time has been far in excess of the expected number of cases from a statistical standpoint. However, a report of these cases is considered worth while, as the problem of malignant tumor of the gallbladder is unquestionably closely related to that of benign cholecystic disease. It is because of this relation between malignant and benign disease of the gallbladder that some of the points to be mentioned, although well known to nearly all physicians, will appear to deal with benign rather than with malignant disease of the gallbladder. When it is considered that between 8 per cent and 10 per cent of adults have gallstones, the importance of the proper concepts regarding the many problems of disease of the gallbladder cannot be overestimated.

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INCIDENCE

Ewing,[1] Erdmann[2] and Kaufmann[3] have stated that carcinoma of the gallbladder is said to comprise 5 to 6 per cent of all cancers seen at postmortem examination. Kaufmann[3] estimated it to be present in 8 to 10 per cent of cases of cancer in females. Various authors have estimated that cancer of the gallbladder ranks fifth or sixth in frequency among cancers of the digestive organs. In a recent monograph on surgery of the gallbladder and the extrahepatic bile ducts, Cutler and Zollinger[4] stated that in the last five years there have been only 6 cases of proved primary malignant tumor of the gallbladder at the Peter Bent Brigham Hospital in Boston. Cooper,[5] in a comprehensive article published in 1937, stated that approximately 2,000 cases of cancer of the gallbladder had been reported in the literature up to that time.

In various reported series of surgically removed gallbladders the incidence of the disease has ranged from 0.5 to 6.5 per cent. It seems safe to say that the average incidence is about 2 to 3 per cent. Marshall and Morgan[6] of the Lahey Clinic, reporting on 1,336 cases of disease of the gallbladder observed from 1928 to 1937, gave the incidence as 1.4 per cent. Smithies[7] reported 23 cases, comprising 2.3 per cent of the gallbladders he had removed. Erdmann,[2] in his survey, found 15 cases of malignant tumors and reported the incidence as 6.7 per cent. Mayo[8] in reviewing 405 gallbladders operated on by himself found 5 per cent with malignant growths. MacCarty[9] surveyed 4,998 gallbladders and found 24, or 0.5 per cent, to be cancerous. At the Mayo Clinic,[10] 89 of 14,978 gallbladders routinely examined after surgical

1. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922, p. 693.

2. Erdmann, J. F.: Incidence of Malignancy in Diseases of the Gall Bladder, Am. J. Obst. **80**:618 (Dec.) 1919.

3. Kaufmann, E.: Pathology, translated by S. P. Reimann, Philadelphia, P. Blakiston's Son & Co., 1929, vol. 2, p. 1002.

4. Cutler, E. C., and Zollinger, R.: Surgery of the Gall Bladder and Extrahepatic Bile Ducts, Am. J. Surg. **47**:185 (Jan.) 1940.

5. Cooper, W. A.: Carcinoma of the Gall Bladder, Arch. Surg. **35**:431 (Sept). 1937.

6. Marshall, S. F., and Morgan, E. S.: Carcinoma of the Gall Bladder, S. Clin. North America **18**:687 (June) 1938.

7. Smithies, F.: Primary Carcinoma of the Gall Bladder: An Analysis of Twenty-Three Proved Instances of the Disease, Am. J. M. Sc. **157**:67 (Jan.) 1919.

8. Mayo, W. J.: Malignant Diseases Involving the Gall Bladder, M. News, New York **81**:1105 (Dec. 13) 1902.

9. MacCarty, W. C.: The Frequency of Strawberry Gall Bladder, Ann. Surg. **69**:131 (Feb.) 1919.

10. Judd, E. S., and Baumgartner, E. J.: Malignant Lesions of the Gall Bladder, Arch. Int. Med. **44**:735 (Nov.) 1929.

removal between 1910 and 1927 showed carcinoma. This is an incidence of 0.59 per cent. Judd and Gray,[11] in a survey of 22,365 gallbladders, found 15,422 with stones and 312 with carcinoma; 212 of the tumors were in the gallbladder itself and 100 in the ducts. This makes the incidence 1.4 per cent if one includes all the carcinomas and 0.9 per cent if one excludes the ductal cancers. Gray [12] mentioned that in recent years the incidence of carcinoma of the gallbladder at the Mayo Clinic has been decreasing, and he attributed this to earlier operation in cases of disease of this organ.

As to sex, Ewing [1] stated that cancer of the gallbladder is much more common in females than in males, the ratio being about 4 or 5 to 1. Kaufmann [3] stated that 90 per cent of cancers of the gallbladder are in females; Judd and Gray,[11] 74 per cent, and Marshall and Morgan,[6] 70 per cent. This is in direct contrast to carcinoma of the ducts, for which the proportion is much higher in males—about 50 per cent or more of carcinomas of the biliary ducts occurring in males, according to Marshall and Morgan.[6] The ratio of females to males in cases of carcinoma of the gallbladder is analogous to the ratio of femles to males in cases of benign disease of the gallbladder.

The age incidence also is similar to that of cancer elsewhere in the body. The tumors usually are found after the age of 40, about 60 per cent being seen between the ages of 50 and 60, although cancer has been reported at both extremes of life. Maxon, cited by Ewing,[1] reported the earliest age, 4 years, while the oldest patient was a woman aged 95, reported on by Kaufmann.[3] Thomas and Norica, cited by Ewing,[1] reported occurrence of the tumor in a woman aged 90.

ETIOLOGY: RELATION TO STONES

As with cancer elsewhere, the cause of cancer of the gallbladder is unknown, but nearly all writers give as the most probable cause an irritative factor based on the relation of calculi to carcinoma. Ewing [1] gave as the modus operandi the following: "Mechanical irritation of calculi, the peculiar form of lipoid metabolism (cholesterin) and the irritative and digestive action of bile seem to combine in producing the remarkable susceptibility of this mucous membrane to cancer." Obviously there are other factors present besides stones, because most patients with gallstones do not have cancer. The role of stones as an exciting factor, however, seems definite. In rare cases adenomas of the

11. Judd, E. S., and Gray, H. K.: Carcinoma of the Gall Bladder and Bile Ducts, Surg., Gynec. & Obst. **55**:308 (Sept.) 1932.

12. Gray, H. K.: Squamous Cell Epithelioma of the Gall Bladder and Liver, Cholecystectomy and Partial Hepatectomy: Report of a Case, S. Clin. North America **14**:717 (June) 1934.

gallbladder may become malignant. Such cases have been reported by Wellbrock [13] and by Marshall and Morgan.[6]

Stones have been found in from 60 to 100 per cent of all cases of cancer of the gallbladder, the figure varying as given from different sources. Kaufmann [3] gave the occurrence of stones as 96.7 per cent; Marshall and Morgan,[6] as 80 per cent, and MacCarty,[9] as 64 per cent. Ewing [1] stated that approximately 4 to 10 per cent of all patients with stone eventually have cancer. Marshall and Morgan [6] stated that in cases of carcinoma of the bile ducts the presence of stones in the gallbladder or in the ducts is not nearly so frequent, occurring in less than one half the cases.

It has been suggested that stones are the result rather than the cause of primary carcinoma of the gallbladder. This seems rather unlikely, for the following reasons: 1. There is usually a history of definite gallbladder colic of several years' duration. 2. Stones removed from gallbladders which have primary malignant growths appear of the "old" variety, as they are firm and usually of moderate or large size. Soft stones and sand are usually not seen, unless in conjunction with the aforementioned variety of stones. 3. Secondary carcinoma of the gallbladder is not nearly so frequently associated with stones. One might argue in this instance that the secondary malignant tumor does not involve the mucosal surface of the gallbladder but affects the serosal surface primarily. 4. In cases of stasis of bile in the gallbladder as the result of malignant tumor in the common duct or in the head of the pancreas, the incidence of stones is about the expected incidence for persons in the age group affected. Marshall and Morgan [6] stated that 4 of 50 carcinomas of the head of the pancreas were associated with gallstones.

SYMPTOMS AND SIGNS

The symptoms of this disorder as a rule are those of chronic cholecystic disease with stones. Pain in the right upper abdominal quadrant seems to be the most outstanding symptom; it is followed by jaundice, indigestion, loss of weight and colic. Pain and jaundice are the two symptoms most frequently seen, one or the other usually being given as the chief complaint. The pain is severe; it is that of gallbladder colic, and it assumes the same typical distribution. It has no relation to the taking of food and usually requires morphine for relief. It is the rare case in which jaundice occurs without pain. After the appearance of jaundice few patients live longer than six months. Other symptoms of indigestion, such as belching, bloating and water brash, are usually

13. Wellbrock, W. L. A.: Adenoma of the Gall Bladder, Am. J. Surg. **23**:358 (Feb.) 1934.

associated with pain or jaundice. Loss of weight occurs as a late symptom. Not uncommonly the liver is palpable well below the costal margin, and a firm, irregular mass may less frequently be felt.

DIAGNOSIS

The diagnosis is made for the most part either at operation or during routine laboratory examination of the removed gallbladder. It is rarely made preoperatively, as most of the patients are thought to have chronic disease of the gallbladder with stones. The occasional patient suspected of having the disease preoperatively may have a large hard mass in the right upper quadrant of the abdomen, below the costal margin, or painless jaundice with loss of weight and anemia. The diagnosis, however, is most difficult to make; therefore, one must depend on operation or the laboratory data. Roentgen examination is of little help in establishing the diagnosis of cancer, although it usually indicates disease of the gallbladder by showing either actual stones or disturbance in function. However, Kirklin [14] mentioned a case reported by Taterka in which the cholecystogram was pathognomonic of carcinoma.

TREATMENT

The treatment in most cases depends on the findings at operation. In many cases abdominal exploration and removal of a specimen for biopsy constitute the only feasible procedure. In exceptional cases, such as that reported by Judd and Baumgartner,[10] a cholecystectomy with resection of the involved portion of the common duct has been carried out. Gray [12] has described a case in which he removed a portion of liver adjacent to the involved gallbladder. Webber [15] has suggested that the grade of malignancy as determined by frozen section at operation may guide the surgeon as to the correct procedure. He suggested that nothing radical should be done for tumors of the higher grades of malignancy. Choledochostomy above the involved segment of duct may be performed as a palliative procedure to relieve jaundice. In the cases in which I have operated choledochostomy appeared of questionable value, although there was usually a temporary improvement in the jaundice with its distressing pruritus.

Certainly when the diagnosis is in doubt operative intervention is indicated, provided the general condition of the patient permits. It is indicated because the diagnosis cannot be established as a certainty without such a procedure, and if too conservative an attitude is assumed

14. Kirklin, B. R.: Cholecystographic Diagnosis of Neoplasms of the Gall Bladder, Am. J. Roentgenol. **29**:8 (Jan.) 1933.

15. Webber, I. M.: Grades of Malignancy in Primary Carcinoma of the Gall Bladder, Surg., Gynec. & Obst. **44**:756 (June) 1927.

by the surgeon, benign disease of the biliary tract, particularly stones in the common duct, may be missed. Something curative may be done in exceptional cases.

PATHOLOGIC PICTURE

There are three main types of carcinoma of the gallbladder: the adenocarcinoma, the squamous cell carcinoma and the mixed adenocarcinoma and squamous cell carcinoma. The first type mentioned is the most common and the second type the least common. Squamous cell carcinoma is assumed to represent a metaplasia of the mucosa of the gallbladder.

Adenocarcinoma is divided into three main types, according to Ewing:[1]

1. The villous, papillomatous or fungating type. This grows from the mucosal surface, eventually distends and obliterates the bladder and forms a bulky, well circumscribed tumor. This type of neoplasm is rarely seen early but may appear as fragile, villous or warty growths invading the gallbladder cavity. Rarely it may grow into the ducts. It may cause hemorrhage and usually produces thickening in the wall of the gallbladder. It tends to attack the surrounding tissues, especially the liver, although it may invade any tissue in close proximity to the gallbladder. In the greatest number of cases stones are found embedded in the mass. This type of tumor is found for the most part near the neck of the gallbladder.

2. The gelatinous type of malignant growth. This forms bulky tumors which infiltrate the wall, fill the cavity of the gallbladder and extend early to the liver, lymph nodes and peritoneum. This type is very rare.

3. The diffuse flat infiltrating carcinoma which begins as a submucous growth or as a thickening or ulceration in the mucosa which has been the seat of chronic inflammation. It invades the wall early, and the gallbladder becomes thick and contracted. It extends to the liver early and may run its course as a secondary hepatic carcinoma in a fair number of cases. In the majority, however, it converts the gallbladder into a hard contracted mass without increase in bulk or constricts it into an hourglass form and fuses it with the adjacent viscera. This type extends early to the surrounding organs (liver, stomach, duodenum and colon), to which it is usually bound by adhesions along which the malignant growth tends to extend. This type may also by direct extension encroach on the ducts and is by far the most common variety seen.

In speaking of the structure of the malignant tumor, it is probable that the markedly scirrhous character of many early cancers of the gallbladder results from the chronic inflammation preceding the new growth, as this is often found in cases of chronically diseased gallbladders with

stones in which there are noted blunt or nodular plaques 2 to 5 mm. in diameter which microscopically show foci of cellular connective tissue surrounding groups of typical glandular epithelium undergoing mitosis. These eventually produce adenocarcinoma of the gallbladder.

CLINICAL AND LABORATORY DATA

There were 5 cases. Four of the patients were women, and 1 was a man. The ages were 52, 62, 62, 69 and 70, with an average age of 63. The duration of symptoms referable to the gallbladder in 4 cases was thirty, eight, five and four years, respectively. In 1 case there were no

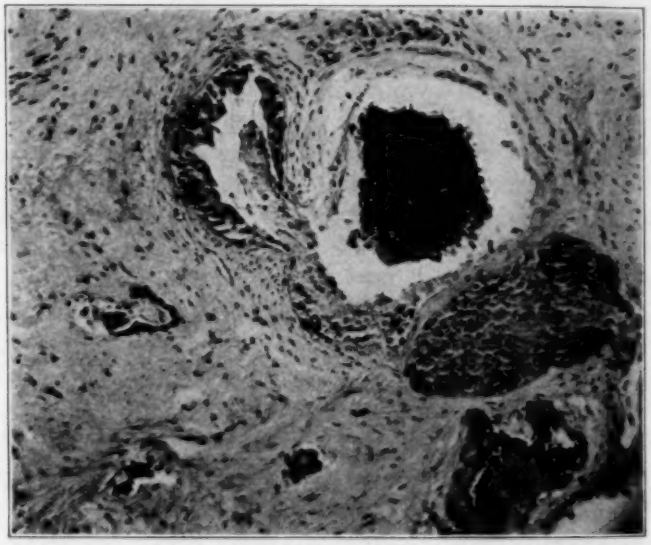

Fig. 1.—Low power photomicrograph of tissue removed from the cystic duct portion of the gallbladder at the second operation. (High cholecystectomy was done for empyema with stones nine months previously, and the gallbladder tissue removed at that time was only inflamed.) The section shows aberrant glandular structures in a dense stroma. Dark-staining calcareous material is present in the lumen of one of the glands.

antedating symptoms referable to the gallbladder (symptoms present for one month only). Rapid loss of weight and jaundice had been observed for one month. In 2 cases there was considerable loss of weight; in the first, 40 to 45 pounds (18 to 20 Kg.) was lost in eight months, and in the second, 20 pounds (9 Kg.) in one month. Slight anemia was present in only 1 case, the value for hemoglobin being 78 per cent. Jaundice was present in all cases at varying times. In 3 cases there was no palpable mass except that representing moderate enlargement of the liver. Cholecystograms in 3 cases showed a nonfunctioning gallbladder

and in 1 case gallstones. In the fifth case only a flat plate of the abdomen was taken on account of the intense jaundice. No stones were visualized in this case. The preoperative diagnosis in 4 cases was gallbladder stones and in 1 case was malignant tumor of the biliary duct.

Fig. 2.—High power photomicrograph of the acinus which is shown in upper left of figure 1. The section shows a pseudostratified arrangement of columnar epithelium, hyperchromatic nuclei and mitotic figures. There are loss of polarity of the nuclei and desquamated cells in the lumen.

The pathologic diagnosis of tissue removed from the gallbladder or of a segment of the gallbladder was adenocarcinoma in all 5 instances (figs. 1, 2, 3 and 4). The duration of life subsequent to primary operation in 4 cases was thirteen months, nine months, six months and seven

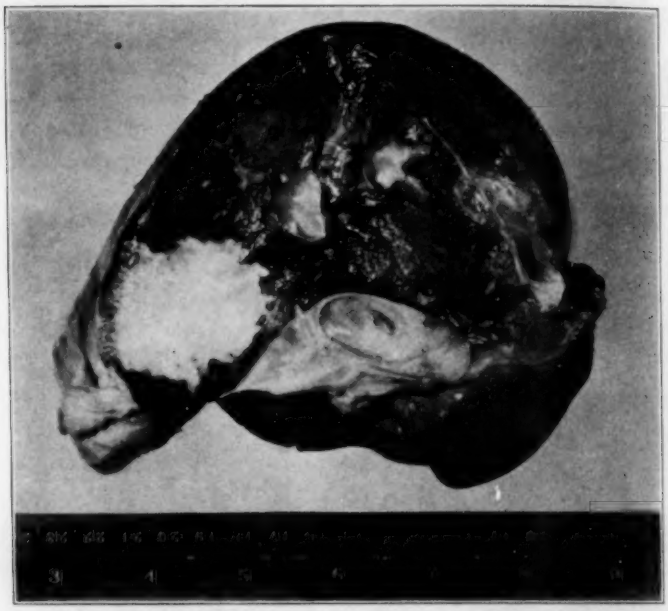

Fig. 3.—Cut surface of the liver at postmortem examination, showing a large carcinomatous nodule in the liver, adjacent to the gallbladder fossa (same case as figures 1 and 2).

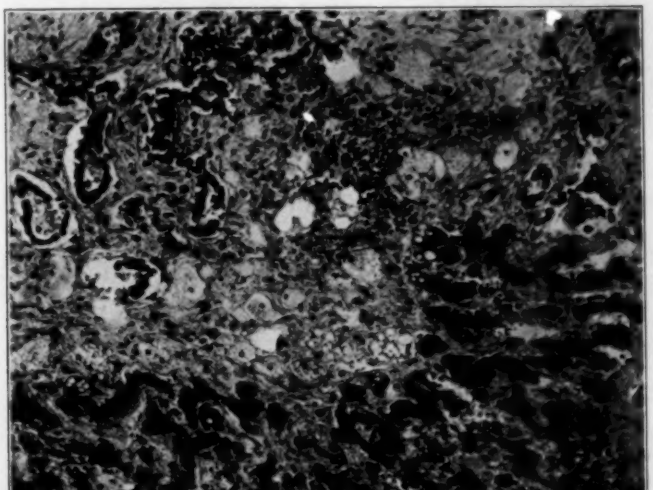

Fig. 4.—Low power photomicrograph of liver at autopsy (fig. 3) showing irregular glandular structures in the upper part and liver cell columns in the lower portion. There is the same tendency to a scirrhous type of structure as was seen in the primary lesion, but not as marked. Endothelial cells containing brown pigment are present at the upper right. The clear vacuolated areas represent degenerated liver cells.

months, respectively. One patient died one week after the operation of renal insufficiency. The average duration of life of patients who survived immediate operation was nine months. The mortality was 100 per cent.

OPERATIVE PROCEDURES

Two patients were operated on once. On 1 of these cholecystectomy was performed; on the other cholecystectomy and choledochostomy.

Three patients were operated on twice. Two of these underwent primary high cholecystectomy for empyema with stones. The gallbladder tissue removed at this operation showed no evidence of malignant tumor. Reoperation in each instance revealed carcinoma in the stump of the gallbladder. A choledochostomy was done in each instance. The third patient underwent primary cholecystectomy and choledochostomy. Several weeks later a secondary operation was undertaken, but the wound was simply closed after exploration, since palliative choledochostomy was technically impossible.

OPERATIVE FINDINGS AND DIAGNOSES

Stones were present in all cases and empyema in 3 cases. In 1 case the patient had a single stone, which was "silent." The diagnosis of cancer by frozen section was made at the operating table in only 2 cases. In the third case carcinoma was observed in the removed gallbladder. In the 2 other cases, in which operation was done for presumed simple empyema and a high cholecystectomy performed, there was subsequent recurrence of symptoms, with jaundice. At reoperation the patients in these 2 cases had primary malignant tumor of the stump of the gallbladder with involvement of the ducts. It is believed in retrospect that malignant tumor was present in the cystic duct portion of these 2 gallbladders at the time of the original operation.

COMMENT

From the history and operative findings in all cases it is undoubtedly true that gallstones antedated the formation of carcinoma in each case. In 3 cases there was superimposed empyema. Involvement of the cystic duct end of the gallbladder with cancer may have caused the empyema in these cases. In every case except 1 the patient had seen a physician several years before for attacks which should have made the diagnosis clear. One patient had undergone roentgen examination about three years prior to operation, which revealed stones. In no case, according to the patient's story, was the patient urged to be operated on prior to the operation performed by me. One patient had been treated symptomatically for years by the family physician.

While, perhaps, one could not argue too strongly for operation on the gallbladder in any case of gallstones on account of the possibility of malignant tumor developing later, there are some other justifiable bases for early operation: (1) to prevent the distress of recurrent colic and dyspepsia; (2) to avoid stone in the common duct with infection and hepatic damage, and (3) to prevent remote visceral degenerative changes. It seems that the possibility of carcinoma could be given as a fourth reason for early operation in such cases.

While early operation on young persons with small stones or even on older persons in whom a stone in the common duct may be missed may result in postoperative colic or even in the necessity of a secondary operation, it seems that early operation has much more to offer than any type of medical treatment. Before early operation is advised in any case, the importance of an accurate diagnosis cannot be overemphasized. It is believed that a history of typical colic is the most important single factor, but in addition there are the physical findings, the laboratory data and particularly the cholecystograms.

It must be borne in mind that there are some cases in which the cholecystogram may be misleading. In some cases, particularly when small stones are present, it may be reported that there is a normally functioning gallbladder without stones. Again, a nonfunctioning gallbladder may be reported in certain cases, particularly of persons who are neurotic and have a low basal metabolic rate. Often, if such a patient is operated on without an adequate history of gallstones, the gallbladder will be found normal anatomically, and the patient will not be relieved by cholecystectomy.

Persons suffering from migraine, chronic nervous exhaustion, chronic constipation and certain functional states, as well as certain organic diseases (which may be either extra-abdominal, such as coronary disease or tabetic crisis, or intra-abdominal, such as the perforating type of peptic ulcer), must be carefully considered in the differential diagnosis.

It seems that unless the patient has some other severe complicating disease operation is clearly indicated. It is surprising how well some persons with some types of complicating severe organic disease stand operations on the gallbladder. Medical treatment with diet, cholagogues, duodenal drainage and the like should be reserved for persons who refuse operative treatment. The risk of a well performed cholecystectomy is about 2 per cent, which may be regarded as about equal to the possibility of development of malignant tumor.

Graham [16] stated that 4 to 5 per cent of women of the cancer age who have gallstones will have carcinoma of the gallbladder and that the

16. Graham, E. A.: The Prevention of Carcinoma of the Gall Bladder, Ann. Surg. **93**:317 (Jan.) 1931.

risk of cholecystectomy is only 1.5 per cent. Hence he expressed the belief that cholecystectomy can justifiably be advised on this basis alone. When one considers other undesirable conditions which patients with gallstones may have or acquire operation certainly is most often the procedure of choice. Among persons who have "silent" stones and later have cancer of the organ there will be necessarily a large percentage in whose cases the malignant growth is unavoidable, since the condition has been entirely asymptomatic until the development of malignancy. However, there will be a certain percentage of patients in whom gallstones are discovered accidentally, i. e., during the course of a pelvic or abdominal operation or during roentgen study.

It seems that advice based on all the clinical and laboratory data available should be given to the individual patient. It is believed that operation will be indicated in most cases of gallstones even of the so-called "silent" variety. Indeed, can one say how long such stones will be "silent?"

Hochberg and Kogut [17] stated that cancer may not be formed by stones but that the same agent or factor in the mucous membrane of the gallbladder which causes stone may be a factor in causing cancer. Be that as it may, from a clinical standpoint stones seem to antedate the carcinoma by some time, and if the cholelithiasis were managed adequately and early it seems that carcinoma of the gallbladder could be prevented in most instances. Some cases of carcinoma of the gallbladder have been reported (Marshall and Morgan; [6] Cooper [5]) in which the gallbladder had been previously drained for stones. In some of these cases multiple drainage operation had been performed for stones, and 1 case was reported in which an interval of fifteen years intervened between the cholecystostomy and the operation which revealed carcinoma in the gallbladder. This would argue for cholecystectomy rather than cholecystostomy when conditions seem to justify such a procedure.

CONCLUSIONS

1. Most frequently the clinical picture of carcinoma of the gallbladder is similar to that of benign disease of the organ, and as a rule a definite diagnosis is impossible without the operative or pathologic data.

2. Most patients with carcinoma of the gallbladder have a history of gallbladder colic of some years' duration, stones being found in almost all cases.

3. The prognosis in most cases of carcinoma of the gallbladder is poor; few patients live more than one year after the diagnosis has been made.

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17. Hochberg, L. A., and Kogut, B.: Primary Carcinoma of the Gall Bladder, Am. J. Surg. **43**:746 (March) 1939.

4. When malignant tumor of the biliary tract is suspected but cannot be proved, operation is justified because (1) some patients will have benign conditions readily amenable to surgical treatment and (2) in rare instances a curative procedure may be carried out even in a case of malignant disease, and frequently a palliative operation may be performed.

5. It is believed that for patients who are good surgical risks early operation for definite benign disease of the gallbladder and even in cases of so-called "silent" stone will reduce the frequency of cancer of this organ.

REVIEW OF UROLOGIC SURGERY

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PROSTATE GLAND

Perineal Prostatectomy.—Davis [27] presented a tabulation of late results after perineal prostatectomy, based on an analysis of replies to questionnaires sent to 100 consecutive patients. Davis [27] was able to maintain a mortality rate of 2.7 per cent in a series totaling 831 consecutive cases of perineal prostatectomy at the time he reported. All the operations were done with the patients under sacral block anesthesia. However, of as great importance as the mortality rate is the matter of late functional results. Most of the men who undergo perineal prostatectomy are in the twilight of life and are interested primarily in comfort. Davis [27] thought it futile to save "a life not worth living (from the point of view of the patient himself) by reason of continued suffering."

In 100 consecutive cases the average age of the patient was about 68.5 years. The average amount of tissue removed was 56 Gm. The perineal wounds closed in an average of sixteen and one-half days, except

27. Davis, E.: Technic and Results in Perineal Prostatectomy, J. A. M. A. 115:582-584 (Aug. 24) 1940.

for two fistulas, which required secondary closure. The postoperative duration of hospitalization averaged twenty-one days. Fifteen patients thought that they urinated too often, and 2 said that they urinated with difficulty. Twenty patients did not have to urinate at night; 41 had to rise once; 33 rose from two to four times, and 6 rose more than four times. On the subject of incontinence 253 additional replies were added to the ones in this questionnaire, making a total of 353. Of these replies, 1 indicated that a patient had complete incontinence; 3 indicated that 3 patients had partial but definite incontinence, and 8 indicated that 8 patients had slight or doubtful incontinence. As judged by the patients' own opinions, 89 of them were well, 10 were improved and 1 was unimproved.

Content of Hormones in Urine During Prostatic Enlargement.—Dingemanse and Laqueur,[28] discussing the content of hormones in the urine in the presence of prostatic hypertrophy, stated that for 13 of 16 patients suffering from prostatic hypertrophy the amount of comb growth–promoting substances excreted per day in the urine was less than 20 international units. In only 3 cases did the amount excreted in the urine reach 50, 44 and 50 international units respectively. The amount of estrogenic substances found in the same urine exceeded 20 international units per twenty-four hours in 1 case only. "The ratio I. U. estrogenic substances: I. U. comb growth substances varied between 0.4 and 2.2," the authors reported. In the absence of prostatic hypertrophy, the urine of 16 men more than 50 years old was examined, and in only 4 cases was less than 18 international units of comb growth substances found in twenty-four hour specimens of urine. In 3 cases the amount of estrogenic substance in the same length of time (twenty-four hours) was less than 40 international units, whereas in 9 cases it exceeded 100 international units. The average amount excreted in the 16 cases was 98 international units per twenty-four hours. In this group the ratio (in international units) of estrogenic substances to comb growth substances was 2 or more in 15 cases. Three patients who had carcinoma of the prostate gland were examined. None of the 3 excreted urine which had an increased content of sex hormones.

Calculi.—Henline [29] stated that many patients suffering from prostatic concretions are symptomless and require no treatment of any sort. When symptoms develop from infection or coexisting adenoma of the prostate gland, the severity of the symptoms or complications resulting

28. Dingemanse, E., and Laqueur, E.: The Content of Male and Female Hormone in the Urine of Patients with Prostatic Hypertrophy, J. Urol. **44**:530-540 (Oct.) 1940.

29. Henline, R. B.: Prostatic Calculi: Treatment by Subtotal Perineal Prostatectomy, J. Urol. **44**:146-168 (Aug.) 1940.

from the prostatic calculi should determine the necessity for treatment. Urethroscopic study and semilateral cystourethrograms may be helpful in determination of the best treatment to employ. Transurethral resection or a punch operation may afford temporary relief but may not cure the patient. Perineal prostatotomy, with removal of some of the calculi, may leave enough calculi to cause recurrence of symptoms or may result in an infected prostate gland, so that recurrence of symptoms would be initiated. Subtotal perineal prostatectomy was described by Henline [29] as a means by which calculi or an infected prostate gland and capsule may be cleanly and completely removed. Complete removal of all the infected glandular tissue with the calculi by subtotal perineal prostatectomy should eliminate the focus of infection and offer a permanent cure without complications. Urinary control was immediate after removal of the urethral catheter from 4 of the 5 patients mentioned by Henline;[29] the fifth patient required about two months to achieve complete control. Rectourethral fistula did not occur, and Henline [29] stated that with proper perineal dissection it should not be a complication.

Carcinoma.—On the basis of a statistical analysis of a series of 677 cases of prostatic carcinoma in which the patients were treated in different ways, Barnes [30] concluded that endoscopic resection of the neck of the bladder is the treatment of choice for symptoms of obstruction and that the subsequent use of roentgen rays has a tendency to postpone recurrence of the growth. The latter opinion, he thought, is substantiated on examination of patients who have lived a year or two after high voltage roentgen therapy and do not show any clinical evidence of carcinoma. Because of these observations it is possible that when the patients more recently treated have been followed for a longer period than at present results of statistical analysis will be more favorable to the patients who underwent transurethral resection followed by roentgen therapy. In this study no patients had undergone total radical perineal prostatectomy. In a comparison of the data on this operation as reported by others with the data presented by Barnes,[30] there is a significant difference in favor of total prostatectomy over any other form of treatment.

Infarction.—Hubly and Thompson [31] reported 3 cases of prostatic infarction studied as to gross and microscopic pathologic aspects and as to the mechanical effects of the lesion as it affects the function of the posterior portion of the urethra. In case 1 there was an early infarction. The authors discussed the experimentally produced volumetric changes

30. Barnes, R. W.: Carcinoma of the Prostate: A Comparative Study of Modes of Treatment, J. Urol. **44**:169-176 (Aug.) 1940.

31. Hubly, J. W., and Thompson, G. J.: Infarction of the Prostate and Volumetric Changes Produced by the Lesion, J. Urol. **43**:459-467 (March) 1940.

in other organs. In case 2 two infarctions may have been present, one rather recent and the other having occurred four years prior to the time of the report. In case 3 multiple infarction was present, with healing by formation of fibrous connective tissue, subsequent contraction and no regeneration. Causes of infarction may be distortion of the vascular supply by adenomatous hyperplasia (Abeshouse), protection against dispersion of local infection, that is, prostatitis (Wilensky), arteriosclerosis, thrombophlebitis or circulatory stasis. The symptoms depend on the mechanical effects, size and age of the infarction.

Sarcoma.—Stevens and Barringer [32] reported on the records of 16 patients who had had prostatic neoplasms diagnosed either clinically or microscopically as sarcoma. The authors included 3 cases of anaplastic carcinoma because it is so readily confused in its history, physical examination and histologic aspects with sarcoma. In 4 cases the initial diagnosis was abscess, and in these cases the prostate gland was explored for pus. Of 5 growths proved microscopically to be myosarcomas, 3 had been diagnosed primarily as benign hypertrophy, and the patients had been subjected to prostatectomy. There were 1 spindle cell sarcoma and 1 lymphosarcoma. In the remaining 6 cases the lesions were regarded clinically as sarcomas. Stevens and Barringer [32] suggested a pathologic classification of only four types, based on the origin of the tumors: (1) myosarcoma, (2) lymphosarcoma, (3) sarcoma of indeterminate origin and (4) anaplastic carcinoma. The literature was reviewed for opinions and examples, particularly in discussion of the histories and courses of patients who had different types of sarcoma of the prostate gland. The less malignant sarcomas (and especially myosarcoma) may suggest benign hypertrophy in older men, who, accordingly, should be subjected to prostatectomy. Sarcoma is most malignant when it affects young persons, and the diagnosis may be suggested by the early age of the patient, the brief history, the increased size of the prostate gland, the elasticity and perhaps the irregularity of contour of the gland without induration, the presence of a suprapubic mass connected with a prostatic tumor and, sometimes, the rapid loss of weight and the presence of cachexia.

Differential diagnosis must be made to exclude abscess, calculus, cyst or carcinoma of the prostate gland, large tumors of the bladder and retrovesical sarcoma. Formation of such a diagnosis is aided by the use of an aspiration needle and by the roentgen ray therapeutic test, as well as by employment of the usual urologic instruments and methods. In practice, Stevens and Barringer [32] wrote, they recognize two groups of cases: first, those in which diagnosis is not made until after prostatec-

32. Stevens, A. R., and Barringer, B. S.: Sarcoma of the Prostate, J. Urol. **44**:83-108 (July) 1940.

tomy for supposed hypertrophy has been done and in which usually a tumor of a low degree of malignancy is actually present; second, those in which unusual and large tumors of high malignancy are present. The experience of the authors and the literature both demonstrate the superior value of irradiation over that of surgical procedures.

Counseller and Bedard [33] reported on 4 patients suffering from sarcoma of the prostate gland who were encountered between 1925 and 1938. In all, 9 such patients have been encountered at the Mayo Clinic, 5 of whom were reported on previously by Bumpus. Of the 4 patients reported on by Counseller and Bedard,[33] the first had a fibrosarcoma; the second probably had a rhabdomyosarcoma; the third had a lymphosarcoma, and the fourth had a leiomyosarcoma. Histologic evidence was presented in support of these diagnoses. In the authors' experience, the treatment of choice for sarcoma of the prostate gland is prostatectomy followed immediately by radium and roentgen therapy.

BLADDER

Tumors.—Ash [34] stated that more than 3,200 cases of epithelial tumors of the bladder are recorded in the Bladder Tumor Registry of the American Urological Association. The pertinent clinical data can be summarized as follows: More than three times as many males as females are affected, and this proportion has been maintained consistently through the years in an increasing number of cases. Age is definitely significant; more than 80 per cent of the tumors occurred in patients more than 50 years of age. There are no epithelial tumors which appear in the first decade, and such tumors are rare before the fourth decade. The youngest patient in the registry was a youth 17 years old at the onset of symptoms; the youngest female patient was a woman 27 years old, but there was some question as to whether her tumor was primary in the bladder. Practically 15 per cent more females than males treated are living without tumor; correspondingly, a similar percentage of males (that is, over females) have either died of tumor or have had recurrence. Hematuria was the primary symptom in about 75 per cent of the cases, dysuria frequently being an associated symptom. More than two thirds of the tumors were situated in the most physiologically active part of the bladder—the posterior wall, including the trigon and the neck. Tumors on the anterior wall were not common. Tumors of the vault are of importance, despite their small incidence, because they are more likely to metastasize than are those in other parts of the bladder. It is probably true also that, since they are situated in a less active portion of the

33. Counseller, V. S., and Bedard, R. E.: Sarcoma of the Prostate Gland, J. Urol. **43**:836-843 (June) 1940.

34. Ash, J. E.: Epithelial Tumors of the Bladder, J. Urol. **44**:135-145 (Aug.) 1940.

bladder, such tumors do not reveal themselves clinically as early as do other tumors and may therefore be more extensive before they are treated.

Judged by ordinary criteria for malignancy, especially metastasis, tumors of the bladder are comparatively benign, but, like papillomas of the larynx, occurring as they do in an important physiologic part, they lead to such serious complications that they are far from benign clinically. More than 50 per cent of patients who had such tumors are dead, yet only about 12 per cent of the entire group of patients suffered from metastasis. In the registry the term "death with tumor" is used advisedly, because the great majority of patients registered did not die of the tumor but of some complicating condition, such as (most frequently) ascending infection of the urinary tract. If the real nature of all the tumors could be determined, it probably would be found that 80 to 90 per cent of them started as papillary tumors. Papillary tumors of the bladder are consistent. Specimens taken from different parts of the same tumor or specimens taken from multiple tumors or from tumors recurring in the course of years may run consistently to type. In conclusion, Ash [34] constructed the following "average case" from the statistics in the registry: The patient is a white man aged 60. The chief complaints are hematuria and dysuria. Cystoscopic examination reveals a single papillary tumor located on the posterior surface of the base of the bladder. Pathologic study reveals papillary carcinoma, grade I or II. The prognosis is repeated recurrence in spite of treatment; the patient has about one chance in three of living five years and about one chance in twenty-five of complete recovery.

Colby [35] stated that there is little evidence to support the contention that malignant tumors of the bladder can be cured by supervoltage irradiation; he discussed the subject from the position of the question whether the tumors really are affected by such treatment. The method is recent, and dosage is still unstandardized. In the group of cases which Colby [35] studied the cancer seemed to have been affected to a greater extent by supervoltage treatment than by other forms of external irradiation with which Colby [35] was familiar. Extensive tumors have regressed to the point of gross disappearance, but there is evidence that even in such a favorable event cancer cells persist in the deep layers of the wall of the bladder. Although the intravesical portions of a tumor may disappear, large portions of cancer can persist in the deep structures and then reappear in the bladder. Such recurrent cancers have responded less well to additional irradiation, and in no instance has the tumor disappeared again after more treatment. The most favorable

35. Colby, F. H.: Supervoltage Radiation in the Treatment of Bladder Tumors, J. Urol. **44**:216-222 (Aug.) 1940.

results have been obtained with patients who had received no previous treatment. Colby's [35] experience during the two years prior to the time of his writing led him to the conclusion that this treatment should be used only for patients suffering from advanced tumors or for old and debilitated patients and that any tumor of the bladder suitable for surgical treatment should be operated on.

Thompson and McDonald [36] reported a case of neurofibroma of the urinary bladder. They stated that neurogenic tumors arising in the genitourinary organs are exceedingly uncommon. They referred to the literature, in which only 3 cases of neurogenic tumor of the bladder are reported. The patient in their own case was a man 59 years old. He had a tumor about the size of a grapefruit which presented between the bladder and the rectum and which could be palpated on rectal examination. The bladder was surgically explored suprapubically, and a large cystic growth was encountered. It was attached to the bladder, near the prostate gland. It was removed and on histologic examination was found to have the typical characteristics of neurofibroma. The immediate postoperative convalescence was uneventful. Sixteen months later the patient was in good health and showed no evidence of recurrence of the tumor.

Carcinoma with Exstrophy.—McCown [37] discussed carcinoma associated with exstrophy of the bladder and added to the scant literature on this subject a case of adenocarcinoma, with complete details and the observations made at necropsy. He reviewed 24 additional cases which he obtained from the literature. In 9 of these 24 cases the treatment was symptomatic or supportive, because of the grave condition of the patients. Four of these patients underwent transplantation of the ureters with excision or extirpation of the neoplasm. Of these 4 patients, 1 died three years later, of metastasis; 1 died within two years, of metastasis; 1 was working six months later, and 1 died on the eighth postoperative day, from ascending infection and uremia. One patient, who underwent extirpation only, was living fifteen months after operation. In 1 case exclusion of the rectum was attempted; the patient died. One patient treated by diathermy, ureterostomy, nephrectomy and cystectomy was recovering at the time of McCown's [37] report. One patient recovered from the Sonnenburg operation but was not traced. In 1 case the neoplasm was removed by electrocautery but recurred; the patient received roentgen therapy and was well five months later. One patient was well three years after cautery excision of the bladder; 1 other patient was

36. Thompson, G. J., and McDonald, J. R.: Benign Tumors of the Urinary Bladder: Report of a Case of Neurofibroma, J. Urol. **43**:831-835 (June) 1940.

37. McCown, P. E.: Carcinoma in Exstrophy of the Bladder, J. Urol. **43**: 533-542 (April) 1940.

well six years and six months after excision of the tumor and application of radium. The best results were achieved by excision, irradiation or a combination of the two.

Diverticulum.—Dees [38] reported and analyzed 95 cases in which vesical diverticulectomy was carried out at the Brady Urological Institute of the Johns Hopkins Hospital. The most common symptoms were those of obstruction of the vesical neck. Infection of the urinary tract was present in all but 7 patients; in 69 of the remaining 88 patients this infection was very severe. The most common cause of obstruction of the neck of the bladder was either contracture of the vesical orifice or formation of a median bar. Slight or moderate prostatic enlargement caused by benign hypertrophy was the next most frequent cause. Transvesical diverticulectomy was carried out in 79 of the 95 cases; extravesical diverticulectomy or a combination of transvesical and extravesical diverticulectomy was done in the remaining 16. In all but 16 cases it was necessary to correct obstruction of the vesical neck in addition to performance of diverticulectomy. The great majority of postoperative complications encountered were caused by infections, epididymitis, pyelonephritis and infection of the wound being by far the most common of these.

In 50 per cent of the cases postoperative urinary drainage continued for more than forty days. Persistent prostatic obstruction was a relatively frequent cause of persistent drainage. Eight patients died in the hospital after the operation. The deaths of 5 of them were caused by pyelonephritis and uremia. The 87 surviving patients were followed for from six months to sixteen years. Of these, at the time of Dees's [38] report, 43 were living and cured; 6 were living and improved; 2 were living and not improved; 16 had died from unrelated causes, and 8 (of whom 5 had carcinoma of the bladder) had died of related causes within a year after operation.

Vesicointestinal Fistula.—Mayo and Miller [39] studied the records of 88 patients with sigmoidovesical fistula. The most common symptoms were frequency of urination, dysuria, chills and fever. Bubbles of gas often were passed through the urethra, usually at the end of micturition, but the passage of feces occurred less frequently. In the presence of a sigmoidovesical fistula the fecal content of the urine is dependent on the state of the stools; when they are firm and the patient is constipated, little or no feces will be seen in the urine; however, if the stools are loose, the quantity of fecal material in the urine will be increased. When the usual flow through such a fistula is reversed and urine is diverted

38. Dees, J. E.: Vesical Diverticulectomy, J. Urol. **44**:466-484 (Oct.) 1940.

39. Mayo, C. W., and Miller, J. M.: Surgical Treatment of Sigmoidovesical Fistulas, Arch. Surg. **40**:897-911 (May) 1940.

into the bowel, laxity of the bowels or chronic diarrhea may result. Cystoscopic examination is essential in formation of the diagnosis. Usually a fistulous opening, often on the left side of the bladder, may be visualized; however, at times this opening is obscured by a mass of granulation tissue or necrotic debris. Gas and occasionally feces may be seen bubbling through the fistula. When a suspicion exists that a fistulous tract is present but when a definite opening cannot be seen, a lead catheter can be passed gently through the suspected region and a roentgenogram made. The shadow cast by the catheter may then be seen in the colon. Force should not be used, because the possibility of creating a false passage thereby is definite. A cystogram may be of help in outlining the fistulous tract. Passage of methylene blue (methylthionine chloride) into the bladder after injection of it into the rectum, or vice versa, is conclusive proof that a fistula is present. Pyelitis and pyelonephritis are not common, despite the frequent occurrence of necrotic cystitis when a sigmoidovesical fistula is present. Mayo and Miller [39] found diverticulitis of the colon (sigmoid flexure) to be the most common cause of sigmoidovesical fistula. Less frequent causes were inflammation, carcinoma and trauma, in the order named. Most of the patients who had diverticulitis complicated by fistula were men (97 per cent), and the average age was 54.8 years. Men are affected more often than women because diverticulitis is more frequent among men. In women the uterus forms an effective barrier between the sigmoid flexure and the bladder. The treatment of choice generally is preliminary colostomy carried out at a site proximal to the lesion. An adequate amount of time should then elapse to permit spontaneous healing of the fistula. This type of healing will occur in certain cases. If healing does not occur, direct surgical attack on the fistula will be necessary. Drainage of the bladder by a suprapubic tube or an indwelling urethral catheter is advisable under these circumstances. Later the colonic stoma can be closed. Single stage operations directed toward excision of the fistula seldom are indicated.

Vesicoappendical Fistula.—Pemberton, Pool and Miller [40] stated that, although vesicointestinal fistula occurs but infrequently, the diagnosis and treatment of this type of fistula comprise one of the serious problems confronting the urologist and the surgeon. The majority of such tracts lead from the sigmoid flexure to the bladder and are the result of perforating diverticulitis of the sigmoid flexure, pelvic inflammatory disease (specific or nonspecific in origin) or carcinoma of the bowel. Kellogg found that the appendix was involved in 27 cases in a group of 592 cases of vesicointestinal fistula. Although variations referable to

40. Pemberton, J. deJ.; Pool, T. L., and Miller, J. M.: Vesico-Appendiceal Fistulas, J. Urol. **44**:274-278 (Sept.) 1940.

the causative factor may be present, the general syndrome presented by patients suffering from vesicointestinal fistula is essentially the same. A history of distress, perhaps acute, in either of the lower abdominal quadrants usually is obtained. Simultaneously with such distress or later, burning and frequency of urination occur. Micturition may occur hourly, and it may be accompanied with scalding pain either during the act or at its completion. With the creation of a fistula, bubbles of gas may be passed through the urethra, and such passage usually occurs at the end of micturition, but the passage of feces does not occur so frequently as the passage of flatus. Cystoscopic study is invaluable in the diagnosis. With vesicoappendical fistula the opening usually is present on the right side of the bladder. Frequently the opening may not be seen, for a mass of granulation tissue or a depressed necrotic region in the bladder may be the only evidence that a fistula exists. When the presence of a fistulous tract is suspected, a lead catheter may be passed through the aperture and a substance opaque to roentgen rays may be injected. The resulting shadows may be seen to outline the fistulous tract and part of the colon.

Five patients who had vesicoappendical fistula have been seen and treated at the Mayo Clinic. Pyuria, varying in degree, was present in all cases. Cystoscopic examination revealed that 2 patients had diffuse inflammatory changes, and a third patient had the same changes (as those of the 2 just mentioned) present at the left base of the bladder. All patients underwent operation. Appendectomy and closure of the opening into the bladder were performed in 3 cases, resulting in 1 death from general peritonitis. Death also occurred in 1 of the remaining 2 cases.

Vesicovaginal Fistula.—Farsht [41] stated that the occurrence of vesicovaginal fistula of surgical origin is on the increase and that vesicovaginal fistula of obstetric origin is on the decrease. The fistula of surgical origin is, as a rule, fixed high in the vagina and is in close proximity to the ureters. The inaccessibility of this type of fistula by vaginal approach makes exposure, proper dissection and repair difficult. Good exposure, careful dissection of the fistulous tract, adequate mobilization of the vesical wall, separate suture of the vesical and vaginal orifices and proper preoperative and postoperative care are essential for successful repair of vesicovaginal fistula. The suprapubic transvesical method of approach allows proper execution of these principles, prevents unsuspected injury to the ureters and permits suprapubic drainage of the bladder, which Farsht [41] said is superior to other types of vesical drainage. This approach also is applicable to the majority of lower-lying fistulas which

41. Farsht, I. J.: Suprapubic Transvesical Repair of Vesicovaginal Fistulas, J. Urol. **44**:279-300 (Sept.) 1940.

result from obstetric injury. An analysis is given of 20 cases of vesicovaginal fistula in which the patients were treated successfully, 3 by the vaginal route and 17 by the transvesical route.

Cystitis Follicularis.—Greene and Feldman [42] defined cystitis follicularis as a rare condition characterized by the presence of true follicles in the mucosa and submucosa of the urinary bladder. At times the renal pelvis and ureter may show similar involvement, and the disease is then designated as pyeloureteritis follicularis. The distinctive feature of this condition from the standpoint of pathologic aspects is the presence of sharply circumscribed lymph follicles which contain germinal centers and which differ in no wise from the solitary follicles of Peyer's patches. In the earlier literature the term "pyelitis granulosa" was applied to this condition. Four causative factors are mentioned in the literature; these are gonorrhea, syphilis, typhoid fever and tuberculosis. Greene and Feldman [42] reported the discovery of cystitis follicularis by cystoscopic study in a mature female dog. The trigon and base of the bladder were covered with small, grayish white nodular excrescences, each surrounded by a red peripheral zone. The nodules varied in diameter from 1 to 2 mm. and appeared to be solid. Gram's stain revealed the urine to contain an enormous number of gram-negative bacilli; growth on eosin, methylene blue and blood agar revealed a pure culture of Escherichia coli. Acid-fast bacilli were not found. Microscopically, sections of the bladder revealed lesions typical of cystitis follicularis.

Emmett [43] considered the problem of retention of urine resulting from imbalance of the detrusor urinae muscle and the vesical neck and recommended treatment by transurethral resection. Exclusive of definite prostatic enlargement, for which the treatment is suprapubic prostatectomy, perineal prostatectomy or transurethral resection, there are other causes of obstruction, which are known as "atypical." Retention is classed as atypical when it occurs in: (1) men too young to be suffering from prostatism; (2) men of the so-called prostatic age who seemingly do not have prostatic hyperplasia; (3) men who have so-called neurogenic bladders, in whom the retention is associated with injury or disease of the central nervous system or of the peripheral nerves, and (4) either young or old in whom the condition has existed throughout their lives, no definite cause ever having been found. In the cases of such men as those last mentioned the condition has been vaguely diagnosed and has been termed, variously and evasively, "congenital atony of the bladder," "atonic bladder," "cord bladder," "neurogenic bladder,"

42. Greene, L. F., and Feldman, W. H.: Cystitis Follicularis in a Dog, Arch. Path. **29**:511-516 (April) 1940.

43. Emmett, J. L.: Urinary Retention from Imbalance of Detrusor and Vesical Neck: Treatment by Transurethral Resection, J. Urol. **43**:692-704 (May) 1940.

"hypotonic bladder" and "urinary retention of indeterminate etiology." Emmett [42] pointed out that if the desire to void is absent, as it is in cases of tabes dorsalis and subacute combined sclerosis, the muscle fibers are overstretched and lose their tone and the detrusor urinae muscle is incapable of expelling the vesical content. Similarly, mild unrecognizable obstruction of the vesical neck or a hypertrophic internal vesical sphincter muscle or one that is unable to relax properly or to coordinate during the act of micturition can easily produce sufficient obstruction for a long period to cause vesical atony and the accumulation of residual urine. The problem of the case in which urinary retention is atypical, according to Emmett,[43] has in the past been attacked from the standpoint of the detrusor urinae muscle. He said that in the past the diagnosis of "atonic cord bladder" depended on the cystoscopic demonstration of: (1) reduction of expulsive force; (2) trabeculation of the bladder; (3) diminution in sensation, and (4) relaxation of the vesical neck, plus the cystometrographic finding of a "hypotonic bladder" and the demonstration of any neurologic lesion, the most common being spina bifida occulta. The real problem involved in these cases of urinary retention of obscure causation was said to be not that of measurement of the actual potential expulsive power of the detrusor urinae muscle, but rather, of comparison of its expulsive force to the resistance that must be overcome by the urine which flows through the vesical outlet. In other words, estimation of the "balance of power" between the detrusor urinae muscle and the vesical outlet seems to be the all-important factor. If the vesical musculature is "weak" or "atonic," whether from neurogenic or from non-neurogenic causes, the problem at hand may well resolve itself into one of weakening of the vesical neck sufficiently to enable the incompetent detrusor urinae muscle to expel the content of the bladder completely. Aside from the common conditions of well defined prostatic hyperplasia and carcinoma of the prostate gland, a vesical neck may become obstructive and may resist the outflow of urine under the following circumstances: (1) when the vesical neck is normal and the detrusor urinae muscle is weak; (2) when coordination fails to occur between the internal vesical sphincter muscle and the detrusor urinae muscle or when the internal vesical sphincter muscle is unable to relax when the detrusor urinae muscle contracts (dysectasia); (3) when hypertrophy of the internal sphincter muscle is present; (4) when inflammation with subsequent fibrosis produces fixation of the vesical neck or contracture of the vesical neck with or without the formation of a median bar; (5) when chronic inflammatory changes are present in the prostatic portion of the urethra, and (6) when there is found a small degree of prostatic hyperplasia that does not appear to be obstructive on cystoscopic examination. These conditions may be extremely difficult

to diagnose cystoscopically even when carefully looked for. In such cases Emmett [43] recommended surgical treatment by a transurethral approach. He stated that if true incontinence does not exist prior to operation in these cases, it will not occur afterward if the external sphincter muscle (compressor urethrae) is not injured at operation. The term "incontinence" must be considered carefully as used in such cases. True incontinence must be distinguished from the overflow type of incontinence. For patients who have the overflow type of incontinence, transurethral resection is the procedure of choice, because this procedure is accompanied with practically no risk to the patient's life. It should be emphasized that transurethral resection must be done completely or the results will be poor. It is not sufficient to remove only one or two pieces of tissue from the posterior vesical lip. In cases in which prostatic enlargement is not present, tissue should be removed from the entire circumference of the vesical neck, so that the internal sphincter muscle will be completely removed. If prostatic hyperplasia is present, as nearly complete a prostatectomy as possible should be carried out.

Emmett [43] then presented 8 representative cases, in which the patients concerned were divided into four types. Under type A were listed patients who had had urinary retention during their entire lives, without any demonstrable neurologic lesion or obstruction of the vesical neck that would account for the retention. Under type B were classified patients who had urinary retention associated with a nonsyphilitic lesion or with injury to the central nervous system. Under type C were listed patients who had urinary retention produced by unrecognized obstruction of the vesical neck, such as contracture, and mild degrees of prostatic hyperplasia. Under type D were listed patients who had urinary retention associated with locomotor ataxia (tabes dorsalis). The functional result obtained in all cases reported in the entire series was excellent.

TESTICLE

Tuberculosis.—Thomas, Stebbins and Rigos [44] stated that tuberculosis of the testicle is not a primary condition and that it rarely occurs when no other genital lesion referable to this disease is present. They reported a case in which genital tuberculosis was localized in the testicle. Tests of the urine for gonadotropin are of value in the differential diagnosis of testicular enlargement. Tests of the blood for syphilis should be made to rule out gumma of the testicle. Aspiration and transillumination eliminate hydrocele and spermatocele. A Mantoux test should be conducted and roentgenograms of the thorax should be made in the presence of intrascrotal tumor. At operation an attempt should be made to

44. Thomas, G. J.; Stebbins, T. L., and Rigos, F. J.: Tuberculosis of the Testicle, J. Urol. **44**:67-73 (July) 1940.

segregate the most strongly suspected tissues for microscopic examination, culture and guinea pig inoculation.

Tumors.—Gordon [45] made a study of the pathologic aspects of 142 primary tumors of the testis. Evidence was presented in favor of the hypothesis that essentially all neoplasms of the testis are of teratomatous origin, with cellular overgrowth of one germ layer often producing homogeneous neoplasms which resemble germinal epithelium. Careful search will reveal teratomatous remains in many characteristic neoplasms of this type, which cannot be distinguished microscopically from those in which teratomatous elements cannot be found. The occurrence of teratomatous elements exceeds the expected incidence or coexistence of two primary neoplasms in the same organ, and the investigator must therefore accept the teratoma as significant of the pathogenesis of tumors of the testis. No stages of transition between normal germinal epithelium and either embryonal carcinoma ("seminoma") or adenocarcinoma were found.

Gilbert [46] analyzed 129 cases of gynecomastia (mammary hyperplasia) associated with malignant testicular tumors. He added 6 cases of his own, thus arriving at a total of 135 cases. He subdivided this total into two groups: group 1 included 103 cases of gynecomastia associated with teratoid tumors, and group 2 comprised 2 of his own cases and 18 cases reported in the literature. Characteristics of the syndrome of choriogenic gynecomastia associated with tumors of the testis were said to consist of: chorionepithelioma in the primary or metastatic tumor; gynecomastia, usually bilateral, with hyperplasia of glandular tissue (often the only clinical symptom present); enlargement or hyperpigmentation (usually occurring together), of the areolas; physiologic activity manifested by either gross or microscopic demonstration of secretion in the breasts, high titers of chorionic gonadotropic hormones and the presence of estrogen; histologic changes in pituitary gland, described generally as "pregnancy cells," and, frequently, hyperplasia of the prostate gland or the seminal vesicles.

Tumors in Mice Receiving Estrogens.[47]—During the course of prolonged treatment with estrogenic substance, the glandular interstitial tissue of the testis in mice of the Strong A strain was observed to become hypertrophied, at times to such a degree that large portions of the testis

45. Gordon, W. G.: Tumors of the Testis: A Study of the Pathology of One Hundred and Forty-Two Cases of Primary Neoplasms of the Testis in Man, J. Urol. **43**:851-858 (June) 1940.

46. Gilbert, J. B.: Studies in Malignant Testis Tumors: II. Syndrome of Choriogenic Gynecomastia; Report of Six Cases and Review of One Hundred and Twenty-Nine, J. Urol. **44**:345-357 (Sept.) 1940.

47. Hooker, C. W.; Gardner, W. U., and Pfeiffer, C. A.: Testicular Tumors in Mice Receiving Estrogens, J. A. M. A. **115**:443-445 (Aug. 10) 1940.

were composed entirely of hypertrophied cells. Recently this change was observed to progress to such a degree as to produce a malignant tumor with metastasis. A mouse 30 days old received weekly injections of 0.05 mg. of estradiol benzoate. After six months the left testis began to enlarge rapidly, and after eight months it was several times normal size. When the animal was killed, the normal structures of the left testis were found to have been entirely replaced by a malignant tumor composed of cords and masses of large vacuolated cells which resembled the hypertrophied interstitial cells previously described. Metastasis to the lumbar and renal lymph nodes had occurred. Histologic changes in the accessory organs of reproduction indicated that these tissues were under the influence of androgenic substance, which suggested the possibility of endocrine activity of the hypertrophied and malignant cells. The right testis exhibited that type of hyperplasia usually seen after treatment with estrogenic substances, but no evidence of malignant tumor. A histologically similar testicular tumor which did not metastasize arose in a second mouse, of the same strain, which received stilbestrol.

Congenital Absence.—Counseller, Nichols and Smith [48] presented 7 cases of monorchia. Absence of the testicle occurred in 4 cases on the left side and in 3 cases on the right side. Study of the cases presented does not reveal any conclusive evidence as to the cause of this condition, nor does it reveal any diagnostic physical signs which will aid in distinguishing anorchidism from cryptorchidism. The importance of the surgeon's bearing this anomaly in mind when he is considering orchidopexy was discussed.

Ectopia.—Hunt [49] presented a case of bilateral ectopia testis pelvicis and discussed the causation, diagnosis and treatment of ectopia. If the testis is intra-abdominal and cannot be palpated, the diagnosis can be made only by operation. Failure of the examiner to make the diagnosis by exploratory operation with ectopia testis in mind probably has resulted in some cases in the incorrect diagnoses of single testis and atrophied undescended testis. The treatment of ectopia testis is surgical correction. In cases in which the true condition has been positively diagnosed by palpation, the operation should be done as soon as the patient has reached an age at which surgical intervention is safe. The intra-abdominally situated testis, which must be discovered by exploratory operation, presents a different problem as to the age at which operation is safe. Hunt [49] said that Johnson's analysis of 544 cases of undescended testes, in which the patients were boys who were prevented

48. Counseller, V. S.; Nichols, D. R., and Smith, H. L.: Congenital Absence of Testis: A Report of Seven Cases of Monorchidism, J. Urol. **44**:237-241 (Aug.) 1940.

49. Hunt, R. W.: Ectopic Testis: Report of a Case of Bilateral Ectopia Testis Pelvicis and Its Surgical Correction, J. Urol. **44**:325-332 (Sept.) 1940.

from having any treatment because of their economic standing, is enlightening in regard to this point. His studies showed that spontaneous descent occurs in about 15 of every 17 cases in which the patients are followed until they reach the age of 16 years and that such descent occurs at the age of 11, 12 or 13 years in three fourths of the cases. The patient who has intra-abdominal ectopia testis obviously belongs to the group comprising the 2 of 17 untreated patients who pass the age of 16 years without the occurrence of spontaneous descent; therefore, if the testis cannot be palpated and has not descended by the time the patient has reached the fourteenth year, exploratory operation should be done. The operation, to be satisfactory, must locate the testis and fix the gland in the scrotum without undue traction of the cord, and it must preserve the blood and nerve supply.

URETHRA

Stricture.—Riba and Harrison [50] discussed the association and incidence (10 per cent) of strictures of the male urethra and Trichomonas vaginalis. They reported 2 cases in which, in addition to strictures and trichomonads, intracellular diplococci were found. A damaged or chronically inflamed urethra with lowered resistance seems to favor the adaptation and local morbidity of trichomonads and to provide a source for dissemination of them.

URINARY LITHIASIS

The first part of Joly's report [51] on urinary lithiasis dealt with the origin and formation of urinary calculi. After a brief survey of the excretion of urine in the various groups of vertebrates, he pointed out that mammals alone excrete hypertonic urine. The concentration of the urine in these animals is undoubtedly a factor which predisposes to the formation of stone. Next, Joly [51] discussed the origin of stone-forming salts in the urine. He pointed out that all such salts exist in a state of supersaturation in the urine and that, although the solubility of these salts is profoundly modified by the p_H of the urine, the presence of other electrolytes and the peptizing action of urea, none of these factors is sufficient to account for the abnormal degree of solubility observed. The action of the urinary colloids was next discussed, and it was pointed out that the abnormal solubility of the stone-forming salts can be accounted for by the theory of adsorption. Adsorption means that the molecules of the sparingly soluble salts are attracted to the surface of the colloid particles and are held there. The effect of this

50. Riba, L. W., and Harrison, R. M.: Strictures of the Male Urethra and Trichomonas Vaginalis, Surg., Gynec. & Obst. **71**:369-371 (Sept.) 1940.

51. Joly, J. S.: The Etiology and Preventive Treatment of Urinary Lithiasis, Internat. Soc. Urol., Rep. (pt. 1) **7**:77-145, 1939.

process is that the solubility of such substances is greatly increased, whereas that of freely soluble salts is unchanged. Formation of a crystalline deposit in the urine occurs in persons in whom the protective action of the colloids is poor. The appearance of this deposit depends on whether it is formed in a colloid solution or in a watery solution. If the former, and if crystals are found in large numbers, it is probable that a stone will form. These forms have been observed in cases of experimental lithiasis, in patients suffering from stone and in the stones themselves. It is only when the stone-forming salts are deposited from, or in, a colloid solution that they can be built up into true calculi. The genesis of formation of stone probably is as follows: The first requisite is that some of the colloid must be precipitated in the form of a gel. The stone-forming salts are adsorbed to the surface of this gel, and crystals are deposited on it. As they form in and around the colloid mass, they take on the atypical form assumed by crystals arising in such a medium. Fresh colloid is deposited on this mass, and fresh crystals are formed on its surface. The laminated appearance of a calculus may be explained by the supposition that the deposition of colloid varies in a rhythmic manner, whereas the deposition of crystals is continuous and uniform.

The second part of Joly's [61] paper dealt with the causation of stone. The question of diet was first discussed, and it was shown that the incidence of stone is most common in districts in which the diet is poor, monotonous and ill balanced. Experimental evidence to suggest that stone may be caused by a deficiency of vitamin A was reviewed. It was also shown that clinical evidence of such deficiency frequently is found among the inhabitants of "stone areas" and that lesser degrees of this type of deficiency, which are recognizable only by means of the test for adaptation to darkness, are common in both England and America. Last, slight degrees of vitamin A deficiency have been recently observed in patients suffering from stone. The effects of infections of the urinary tract, of metabolic disorders and of either general or local diseases were next considered. Emphasis was laid on increased elimination of calcium salts in the urine in cases in which the patient is immobilized or suffers from injury or disease of bone or from hyperparathyroidism, and the relation of these conditions to phosphatic lithiasis was discussed. After a brief review of Randall's theory that stones arise from the "milk patches" occasionally found on the renal papillae, the relation of calculous disease to the uric acid infarcts of infants and the influence of renal anomalies on formation of stone were discussed. The geographic distribution of stone was next considered, and it was shown that the soil, the water and the climate can have little influence in determination of the relative frequency of lithiasis. It was also pointed out that, although the disease as seen in Asia does

not show any indications of change, it has altered remarkably in western Europe during the last fifty or one hundred years. Stone in the bladder in children has become rare, whereas renal lithiasis probably is increasing in frequency. The diminution of formation of stone in childhood was ascribed to better and more hygienic feeding; the cause of the increased frequency of renal lithiasis was stated to be unknown.

The third part of Joly's [51] paper dealt with the preventive treatment of calculous disease. This subject was discussed on general principles. It was emphasized that the incidence of stone in Asia can be greatly diminished by improvement of the social conditions under which the inhabitants live, by enrichment of their diet and by the teaching of the rudiments of hygiene. The disease is thus a problem for the state rather than for the individual physician. It is also possible that the incidence of stone in western Europe may be diminished by measures introduced to improve the general social condition of the people, but Joly expressed the opinion that this is a problem for the future.

In Rydgaard's [52] report in a symposium on stone he stated that the term "primary urinary calculus" is to be understood as meaning "a calculus in a healthy system with sterile urine." He presented a summary of the various theories of the cause of the formation of urinary calculi and of the results up to the time of his writing of experimental formation of calculi; material to illustrate primary urinary calculus was presented. Primary urinary calculi are principally unilateral renal or ureteral calculi. Distribution of them between the right and left sides is 1:1, and between male and female patients, 7:3. Every stone consists of organic and inorganic substance. The inorganic substance is often calcium oxalate, but uric acid, urates and phosphates also occur often. Supersaturation of the urine with crystalloid must occur for the formation of a concretion to take place. On determination of the degree of saturation of the urine, attention must always be paid to the influence of all the urinary electrolytes on each other, by means of which the degree of saturation, which often seems high if this influence is disregarded, is generally considerably reduced. The urinary colloids are of no importance to the solubility of the urinary crystalloids but seem to influence precipitation of such crystalloids and the speed with which it takes place.

Attempts to form calculi experimentally, together with a number of clinical observations, indicate that diet is of extraordinary significance in the formation of primary calculi. In particular, the ingestion of large quantities of ingredients that contain oxalic acid or purine and deficiency of magnesium, calcium and vitamin A (perhaps also of vitamins B, C and D) seem to be able to cause the formation of calculi, which is also

52. Rydgaard, F.: The Aetiology and Preventive Treatment of Primary Urinary Calculus, Internat. Soc. Urol., Rep. (pt. 1) **7**:146-185, 1939.

influenced by various conditions which, acting through changes in metabolism, increase the excretion of oxalate, purine or phosphate. The last is encountered in cases of hyperparathyroidism. Various investigations and facts seem to indicate that something else, not yet ascertained, in addition to supersaturation of the urine (which is an indispensable factor in the formation of every calculus), is necessary. The hypothesis is proposed that this unknown cause may be damage to the kidney itself. Since the cause or source of the hypothetic calculus-forming factor in the kidney itself is not known, the greatest importance in preventive treatment must be attached to prevention of supersaturation of the urine with crystalloids. This prevention is attempted by administration of a sufficiently mixed diet. Food containing oxalic acid and purine must be avoided. The ingestion of liquids must be fairly plentiful, and care must be taken that there is a sufficient content of soluble, absorbable calcium and magnesium salts and also of various vitamins. Prevention of recidivation after treatment for primary urinary calculi is a part of the preventive treatment. This demands careful removal of the original stone or stones and treatment of possible abnormalities within or without the urinary system (for example, parathyroidectomy). Postoperative treatment by means of diet and, if necessary, medicine should then follow, the p_H of the urine, its content of crystalloids and so forth, in accordance with the nature of the original stone, being constantly checked.

Randall,[53] in a discussion of the causation of primary renal calculus, stated that in the absence of stasis primary renal calculus is dependent on, and arises because of, a pathologic condition of the renal papillae. This pathologic condition is a varying degree of damage to the structures of the collecting tubules and the supporting interstitial tissue, and this damage is succeeded in living persons by attempted repair, in which process calcium salts may be deposited. Deposition of calcium salts may be both intratubular and extratubular and may occur in varying degrees; in some cases it is slow, discrete and chronic; in others, acute, rapid and overwhelming.

On the basis of Randall's studies at necropsy, two types of calculous disease are distinctly discernible: In type 1 a calcium plaque with a predominance of interstitial deposition occurs, and it evidences a slow, chronic process; in type 2 intratubular deposition occurs, producing the picture of a more drastic process and more rapid accumulation. In calculous disease of type 1 calcium carbonate and calcium phosphate have been identified, and it was suggested that calcium nucleinate may be the remainder. In calculous disease of type 1 the deposition of salt occurs most frequently on the side wall of the papilla, and such deposition

53. Randall, A.: The Etiology of Primary Renal Calculus, Internat. Soc. Urol., Rep. (pt. 1) **7**:186-261, 1939.

remains innocent of any part in the causation of stone until growth and pressure (decubitus) bring a plaque of calcium to the surface of the papilla. When such a calcium plaque does become exposed on the surface of the papilla, it is then bathed in calicinal urine and, acting as a foreign body, becomes the nidus on which any urinary salt may crystallize. Calculi of both calcium phosphate and calcium oxalate have been identified as having such origin and growth, and it is to be expected that other salts will be so identified in the future, when technical difficulties have been overcome. On this pathologic basis it can be recognized how a stone gains an opportunity to grow and also how it can remain asymptomatic for long periods. Evidence was presented to show that when a calculus is extruded extrusion is accomplished by tearing from the papilla its foundation of deposit of calcium salts.

In calculous disease of type 2, calcium salts are principally intratubular and may present all gradations, from simple tubular inspissation to drastic choking of tubules and marked tubular damage, with some interstitial deposition in cases in which the condition is advanced.

Randall [53] presented the results of 1,154 studies at necropsy, in which lesions of type 1 were observed in 19 per cent and lesions of type 2 in 1.9 per cent and in which 65 examples of the formation of calculus adherent to the renal papillae were observed.

Randall presented evidence based on hyperparathyroidism in 3 human beings and 32 dogs given parathyroid extract to show that in this condition the initial renal damage is to the epithelium of the tubules and that it precedes the characteristic deposition of calcium salt. Randall [53] concluded that in the course of its normal function the kidney suffers insults from many directions and that the greatest damage therefrom occurs in the convoluted and especially in the collecting tubules of the renal papillae, where the greatest concentration of both normal and abnormal urinary elements occurs. On the basis of these research studies, Randall [53] has been able to prove that primary renal calcification is a reparative response to certain morbid states in the renal papillae, that damage to the epithelial cells lining the renal tubules occurs early and that this damage is the prime essential to the subsequent permanent deposition of calcium salts. Randall [53] suggested that the salt deposited in the form of a calculus will be the salt most ready to crystallize out of solution, whether such crystallization is due to abundance, to disturbed colloidal balance or to the poorly understood laws of crystallization. In Randall's paper there were offered for the first time suggestions as to the common origin of the diversification of chemical constituents of stone, together with an explanation of where, why and how a stone forms, and also an accounting for the static and asymptomatic state during which a stone slowly gains growth.

On the basis of published reports, hyperparathyroidism may be expected to account for not more than 5 per cent of the cases in which clinical primary renal calculus is present. That hypovitaminosis A can be responsible is to be recognized, but in modern civilization it probably can account for but a small portion of the remaining 95 per cent of cases, and it would be generous to credit it with as much as 10 per cent of the cases of primary renal calculus. It was Randall's belief that the products (toxins) of distant focal infection play a major role in the causation of papillary pathologic processes and the causation of stone. The close relation that exists between the so-called calculus age and that during which focal infections occur—25 to 50 years—never has been pointed out, and, although results of clinical studies are too uncertain to be trusted, it was Randall's [53] constant observation that patients who had primary renal calculi consistently had active focal infectious conditions elsewhere. The undoubted fact that toxins other than bacterial (toxins of disease, metabolism or dehydration) may produce a similar renal response must not be forgotten.

The treatment and prevention of primary renal calculus embrace a broad study of the individual patient, an intelligent analysis and control of his urine and the correction of pertinent factors, most of which are distant from the seat of disease.

Harrington [54] reported a clinical study of 480 cases of urinary lithiasis in which the patients were observed in the University of California Hospital. During the first five years calculi were removed from 73 patients, with 2 deaths; nephrectomy was required in 16 cases, with 1 death. The total mortality rate for removal of calculi, regardless of method, from the upper part of the urinary tract was 3.37 per cent. During the last five years calculi were removed from 100 patients, with 4 deaths, and nephrectomy was employed in 34 cases, with 1 death. The total mortality rate was 3.65 per cent. The rate of recurrence has been substantially reduced in the last five years. The increased use of roentgen rays at operation in cases of multiple lithiasis undoubtedly has been a great factor in such reduction. The general rate of recurrence after removal of stones from the kidney by all methods was 18.6 per cent during the first period and 10.9 per cent during the second period.

Flocks [55] stated that in the outlining of a regimen for the prophylaxis and medical management of calcium urolithiasis, the factors of vitamin A deficiency, focal infection, infection of the urinary tract, stasis of the urinary tract, precipitability of urinary calcium and urinary excretion of calcium must all be considered. Flocks [55] discussed the

54. Harrington, H. L.: A Clinical Study of Four Hundred and Eighty Cases of Urinary Lithiasis, J. Urol. **44**:507-519 (Oct.) 1940.

55. Flocks, R. H.: Prophylaxis and Medical Management of Calcium Urolithiasis: The Role of the Quantity and Precipitability of the Urinary Calcium, J. Urol. **44**:183-190 (Aug.) 1940.

urinary excretion of calcium in the normal person and under pathologic conditions. The relation of such excretion to calcium urolithiasis was emphasized, and a regimen for the management of calcium urolithiasis based on the urinary excretion of calcium was described. The significance of the precipitation of calcium in the urine in relation to calcium urolithiasis was discussed. A method for determination of the quantity of calcium in the patient's urine was described. The results for a small group of normal persons and patients with urinary calculi were given. These emphasized the necessity of following the effects of therapy on the precipitation of calcium in the urine.

Effect of Alkalis.—Eisele [56] discussed the role of alkali therapy for peptic ulcer in the formation of urinary calculi. In a series of 505 patients who had kidney or ureteral stones, there were 43, or 8.5 per cent, who suffered from preexisting treated peptic ulcers. There were 13 additional patients, or 2.6 per cent, who had chronic gastrointestinal complaints for which they habitually took alkalis. Thus, there were 56 patients, or 11.1 per cent, for whom the ingestion of alkali powders may have been considered of etiologic importance in the formation of their urinary stones. This is in agreement with theoretic considerations and constitutes the clinical counterpart of experimental production of stones in laboratory animals by the feeding of crystalloids. Eisele [56] expressed the opinion that the hyperexcretory calculosis which developed among these patients demonstrates the potential danger of alkali therapy for peptic ulcer.

Turell [57] stated that urolithiasis may be produced by extrarenal foci of infection or on the basis of preexisting infection of the urinary tract. Urinary infection caused by organisms of the colon bacillus group may be an important factor in the genesis of urolithiasis. Inflammatory and suppurative lesions of the anorectocolonic tube and dysfunction (stasis of fecal current) were considered to be important foci of infection. The colon also may act as a portal of entry for enteric organisms into the blood and lymph streams. Eradication of these lesions and correction of dysfunction are important parts of the therapeutic program for the elimination and prevention of urolithiasis with infection caused by the organisms of the colon bacillus group.

CYSTINURIA

Hammer and Thompson [58] reviewed the literature and reported on the patients suffering from cystine lithiasis encountered at the Mayo

56. Eisele, C. W.: Role of Alkali Therapy for Peptic Ulcer in Formation of Urinary Calculi, J. A. M. A. **114**:2363-2366 (June 15) 1940.

57. Turell, R.: The Intestinal Phase in Urologic Disease: III. The Rôle of the Colon in Urolithiasis, J. Urol. **43**:476-480 (March) 1940.

58. Hammer, H. J., and Thompson, G. J.: Cystine Lithiasis: A Clinical Study, Urol. & Cutan. Rev. **44**:341-355 (June) 1940.

Clinic during the years 1930 to 1938 inclusive. During this period 16 instances of cystine lithiasis and 5 instances of cystinuria without lithiasis were recognized. It seems likely, Hammer and Thompson [58] wrote, that many instances of cystinuria were not detected. The authors stressed the importance of obtaining a familial history when the diagnosis of cystine lithiasis is to be made. The test used to determine the presence of cystine in the urine is Osterberg's modification of the Sullivan test. It is performed as follows: To 5 cc. of urine add about 0.3 cc. of a 50 per cent solution of hydrochloric acid (or add the acid until the urine reacts acidly to congo red paper). Then add 2 cc. of fresh 5 per cent solution of sodium cyanide. Mix and let reduction proceed for ten minutes at room temperature; then add 1 cc. of fresh 0.5 per cent solution of 1, 2-naphthoquinone-4-sodium sulfonate. Mix and add 5 cc. of 10 to 20 per cent solution of anhydrous sodium sulfite in 0.5 normal sodium hydroxide. Mix and let stand for thirty minutes. Add 1 cc. of a 2 per cent solution of sodium hyposulfite in 0.5 normal sodium hydroxide. If a red color forms, cystine is present. Usually, seven standards are prepared in a similar manner for quantitative determinations.

Hammer and Thompson [58] advocated employment of a low cystine diet and alkalinization of the urine in the treatment of cystine lithiasis. They also recommended surgical removal of the calculi. Of the 16 patients studied, 12 were males. The average age at which onset occurred was 16.4 years. Pain was the most common symptom. A history of the passage of gravel was obtained from 13 of the 16 patients. Twelve patients had or had had bilateral calculi. In each case a positive response to the test for cystinuria was obtained. The calculi cast opaque shadows in the original roentgenogram of the urinary tract in 12 of the 16 cases. In the 4 other cases calculi had been passed by the patients at some previous period, and the urine contained cystine. Retrograde or excretory urographic study did not reveal any evidence of lithiasis in these instances. Alkalis and diets (low protein, low cystine and alkaline ash) were advised for all patients. Postoperatively, immediate alkalinization seems advisable to prevent early recurrence.

BACILLURIA (MYCO. TUBERCULOSIS)

Rosencrantz [59] made a urologic study in 200 cases in which proved chronic pulmonary tuberculosis had afflicted men. The genital tract was examined, and guinea pigs were inoculated with urine.

Tuberculosis of the epididymis was found 41 times and tuberculosis of the seminal vesicles 5 times, always in conjunction with tuberculosis

59. Rosencrantz, E.: Frequency of Tubercle Bacillus in Urine of Chronic Pulmonary Tuberculosis in Relation to Urogenital Complications, J. Urol. **44**:498-506 (Oct.) 1940.

of the epididymis. Tuberculosis of the prostate gland was not found clinically; in 1 case it was observed microscopically after necropsy. McKenna and Sweany found this condition in 4.2 per cent of their cases of advanced pulmonary tuberculosis. According to the views of Thomas and Kinsella, the kidney is first infected, and this causes Myco. tuberculosis to appear in the urine; the prostate gland is then involved; there, in turn (via the prostatic ducts) the seminal vesicles are infected, and then the epididymis is infected, despite the fact that clinically only the epididymis seems involved. Tuberculosis of the kidney combined with tuberculosis of the epididymis was found in only 1 of 41 cases studied. Mombaerts and Laroche were said to have found combined renal and genital lesions in 31 per cent of their 184 cases of renal tuberculosis. Hobbs, in 1,000 cases of pulmonary tuberculosis in which study was carried out at necropsy, observed renal lesions in 16.2 per cent. The low incidence in Rosencrantz' [59] paper may be explained by the fact that the study was essentially a clinical one; studies carried out at necropsy doubtless would have increased the percentage of renal involvement.

INFECTIONS OF THE URINARY TRACT

Austen [60] stated that since in cases of infection of the urinary tract sulfanilamide directly exerts the effect of an antiseptic agent on the organism, direct instillation of the drug into the renal pelvis should be of value in certain cases, particularly those in which the patient tolerates the drug poorly when it is administered by the usual routes; those in which renal function is reduced; those in which there is an anatomic or pathologic abnormality which prevents high local concentration of the drug, and those in which there is interference with renal drainage. Austen [60] presented the results of treatment of 10 patients who had infection of the upper part of the urinary tract. Direct instillation of a sulfanilamide compound (sulfanilamide with maltose) into the renal pelvis was done. When the drug was administered in this manner, it was well tolerated in all except 1 case. A definite clinical and bacteriologic improvement was noted in 8 cases, a bacteriologic cure was obtained in 1 case, and no improvement resulted in 1 case. Observations on the concentration of sulfanilamide in the blood, in urine obtained from the treated kidney and in urine obtained from the untreated kidney, demonstrate that the drug is absorbed from the renal pelvis into the blood stream in appreciable amounts and that it is also excreted in the urine from the kidney into which no injection was made. The concentration of sulfanilamide in urine from the kidney into which the drug was injected reaches a much higher value than is possible when the drug is

60. Austen, G., Jr.: Pelvic Lavage with Sulfanilamide in the Treatment of Renal Infections, J. Urol. **43**:637-653 (May) 1940.

administered by the oral or the subcutaneous route. As a result of these observations, Austen [60] said that although it is a method of administration which has definite limitations, direct pelvic instillation of sulfanilamide is a worth while procedure in selected cases of renal infection.

The type of infection present and therefore the mode of treatment to be instituted may be determined readily in cases of infection of the urinary tract by use of a simple type of Gram's stain. This stain demonstrates the type of organism present (coccus or bacillus) and its reaction (positive or negative). Cook and Sutton [61] stated that the majority of infections of the urinary tract are caused by gram-negative bacilli (E. coli [predominantly]; Aerobacter aerogenes; Pseudomonas; Salmonella; Proteus; Shigella; Alcaligenes). Further differentiation of these may be done on eosin–methylene blue agar plates. All yield to the same therapeutic attack (acidification with mandelic acid and similar agents) except Proteus, a urea-splitting organism which causes a high urinary p_H. Cocci cause 20 per cent of all urinary infections, which, excepting those caused by the gonococcus, are caused by gram-positive organisms. A simple stain will distinguish Streptococcus faecalis from all other streptococci and all streptococci from staphylococci and micrococci. Special mediums are necessary for growing the cocci. Pathologic changes depend on (1) virulence of the organism, (2) degree of infection and (3) resistance of the patient. However, the type of organism present is to a certain extent a factor. E. coli, A. aerogenes and Proteus produce progressively deeper and more ineradicable lesions. Therapy with mandelic acid will cure all these infections, including those due to forms of the Proteus genus when such forms do not have the power to split urea. Eradication of both coincidental pathologic deformity, whether primary or secondary to the infection, and focal infection is important, particularly in the prevention of urinary stagnation. It is doubtful whether Pseudomonas is ever a primary invader. Str. faecalis, the most common form of coccus in relation to urinary infection, is, when it is found in this particular type of infection, almost invariably secondary to nephrostomy or manipulation. Micrococci clinically may be pathogenic, and eradication of them may result in complete symptomatic relief. Cocci characteristically produce greater deformity of the ureters than of the pelves; the converse is true of bacilli. Mandelic acid causes fewer untoward reactions than does sulfanilamide, but the latter is better for attack on urea-splitting organisms or for therapy in cases of impaired renal function, even when bacilli are the causative organisms. Str. faecalis responds better to mandelic acid therapy, but other coccic infections should be treated with sulfanilamide or neoarsphenamine (administered intravenously) plus acidification. Treat-

61. Cook, E. N., and Sutton, E. B.: Infections of Urinary Tract, with Particular Reference to Causative Organism, J. Urol. **42**:880-885 (Nov.) 1939.

ment of associated pathologic conditions is very important; release of urinary stagnation is especially important. Against the gonococcus, which has its own characteristics on smear and culture, sulfapyridine is the drug of choice.

GONORRHEA

Arthritis.—Culp [62] studied a series of 200 cases of gonorrheal arthritis in an effort to determine the most satisfactory form of therapy. His cases included 105 in which the condition was acute, 50 in which it was subacute and 45 in which it was chronic. Of the forms of treatment employed, those in which sulfanilamide, mercurochrome (the disodium salt of 2,7-dibromgammahydroxymercurifluorescein) administered intravenously and fever therapy were used gave the best results. Sixty-nine per cent of the 29 patients treated intravenously with mercurochrome were discharged well or markedly improved. Excellent results were obtained with patients who had chronic and subacute conditions, as well as with those who had acute conditions. The dose varied from 10 to 30 cc. No serious reactions were encountered. Generally only three or four doses were required. When the initial doses were small, the number required was usually greater. Only 53 per cent of the 19 patients who received fever therapy became well or markedly improved. Several patients had severe reactions, and 1 died while undergoing treatment. Cures were effected in the chronic as well as the earlier stages. This treatment, Culp wrote, is strictly a procedure to be used in hospitals and has definite contraindications. Twenty-two patients were treated with sulfanilamide, and 68 per cent of these left the hospital well or markedly improved. In most of the cases the condition was acute, and the patients showed amazing improvement, despite osseous changes in a few instances. The total dose varied from 14.4 to 105.6 Gm., and the duration of therapy varied from three to twenty-two days. Values for the content of the drug in the blood of the patients were followed in most cases and varied from 2.8 to 20 mg. per hundred cubic centimeters. Most of the patients had mild toxic symptoms; anemia developed in 6; 1 required a transfusion of blood, and in another marked leukopenia developed. No fatalities resulted.

Chemotherapy appeared to be more efficacious than any of the other forms of treatment. Sulfanilamide and mercurochrome (administered intravenously) were recommended by Culp [62] for the routine treatment of gonorrheal arthritis, and each seemed to him to be of about the same therapeutic value. Both often produced surprisingly rapid cures. Fever therapy was of marked benefit in some cases, but reactions to it were more severe than to other forms of treatment. It was not condemned

62. Culp, O. S.: Treatment of Gonorrheal Arthritis: An Analysis of Two Hundred Cases, J. Urol. **43**:737-765 (May) 1940.

on the basis of the small group of cases reported by Culp, but it was said to involve more risk than other forms of treatment and also was said to be much more heroic than the chemical methods. The initial dose of mercurochrome should be 15 cc. of a 1 per cent solution, followed by 17, 19 and 21 cc. after intervals of three or four days or longer, according to the reactions produced. A sharp increase in temperature may be considered the equivalent of the production of antibodies or of a defense reaction and is of therapeutic value. Sulfanilamide should be administered in doses sufficient to maintain a content of the drug in the blood of 8 mg. per hundred cubic centimeters if possible. This can be accomplished most readily by administration of 1.2 Gm. (about 20 grains) with an equal amount of sodium bicarbonate every six hours until the desired concentration in the blood has been reached. The subsequent maintenance dose of the drug may be increased or reduced according to the indications provided by the content of the drug in the blood and the therapeutic effect on the arthritis. Sulfanilamide rarely should be administered for longer than two weeks, and careful chemical studies of the blood should be made at frequent intervals (daily, if possible) during treatment.

Roth [63] stated that in 47 per cent of 44 cases of acute gonorrhea in which patients were treated with sulfanilamide cure resulted in two weeks or less and that in 22 cases of acute gonorrhea in which patients were treated with sulfanilylsulfanilamide (paraaminobenzenesulfonylparaaminobenzenesulfonamide) cure resulted in 73 per cent. In 42 cases of acute gonorrhea in which private patients were treated with sulfanilamide plus irrigation with acriflavine hydrochloride and potassium permanganate, 71 per cent of the patients were cured within two weeks or less; in 29 cases of acute gonorrhea in which private patients were treated with sulfanilylsulfanilamide plus daily irrigation with acriflavine hydrochloride and potassium permanganate, 92 per cent of the patients were cured within two weeks or less.

Twelve patients who did not respond to therapy with sulfanilamide were cured when sulfanilylsulfanilamide was employed. The dose of sulfanilamide never was more than 45 grains (3 Gm.) a day. The routine dosage of sulfanilylsulfanilamide was 45 grains (3 Gm.) in the outpatient department of the department of urology of Ohio State University at Columbus, Ohio, and in the treatment of private patients it was 45 grains (3 Gm.) the first two days and 30 grains (2 Gm.) daily thereafter. Neither drug was administered for more than two weeks. Roth [63] stated that his experience has proved that sulfanilyl-

63. Roth, L. J.: Sulfanilyl-Sulfanilamide (Disulon) Versus Sulfanilamide in the Treatment of Acute Gonorrhea in the Male, J. Urol. **43**:483-490 (March) 1940.

sulfanilamide is superior to sulfanilamide in attacks on the gonococcus. When response to either sulfanilamide or sulfanilylsulfanilamide is not immediate, clinical cure is prolonged by from four to six weeks, and it may be wise, Roth suggested, to discontinue chemotherapy and to employ other methods of treatment to prevent the occurrence of unnecessary toxic effects referable to prolonged administration of whichever drug is used. Reactions produced by sulfanilylsulfanilamide (noticed in 25 per cent of cases) were much less than those produced by sulfanilamide (noticed in 60 per cent of cases). The complication of peripheral neuritis was observed in only 1 of the 63 cases in which patients were treated with sulfanilylsulfanilamide.

SULFANILAMIDE AND DERIVATIVES

Sulfanilamide.—Sickler [64] stated that after the oral administration of sulfanilamide the drug is excreted by the kidney in a quantity sufficient to render the urine bactericidal for most organisms commonly found in the presence of infections of the urinary tract. At a given p_H, the intensity of the bactericidal effect appears to be directly proportional to the concentration of the drug in the urine. The reaction of the urine is a factor of major importance. When the same concentration of sulfanilamide was maintained constantly, more favorable bactericidal results were demonstrated in alkaline urine at p_H 7.7. Bacteriostatic or bactericidal effects were observed in 79 per cent of tests on forty-three strains of organisms in specimens of urine of p_H 7.7 containing 80 mg. of the drug per hundred cubic centimeters. Different strains of the various organisms tested were not equally susceptible to the same concentration of sulfanilamide in the urine. Nine of the forty-three strains mentioned were resistant to the bactericidal effect of 80 mg. of sulfanilamide in 100 cc. of urine at p_H 7.7. Increase of the concentration to 200 mg. per hundred cubic centimeters (an increase of more than 100 per cent) affected only three of the nine resistant organisms. In view of the known toxic manifestations which this drug causes, the maintenance of such high urinary concentrations of sulfanilamide, in the opinion of Sickler,[64] is only rarely justifiable.

Growth of bacteria was not inhibited in urine which had a p_H of less than 9.5. At this level members of the colon, aerogenes, Salmonella and Pseudomonas groups were killed. Staphylococcus aureus and Proteus vulgaris were not affected by this degree of alkalinity. Since the maximal alkaline titer in urine from human beings never approaches such a figure, alkalinity alone has no bactericidal value in the treatment of infections of the urinary tract.

64. Sickler, J. R.: A Study of the Bactericidal Activity of Sulfanilamide in Urine at Various Levels of Hydrogen Ion Concentration, J. Urol. **43**:906-916 (June) 1940.

Sulfathiazole.—Culp [65] reported results obtained in the treatment with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) of 30 patients who, among them, had a great variety of infections of the urinary tract. In 24 cases an attempt was made to sterilize the urine completely. The result in 16 (66.7 per cent) was elimination of all infection. Three patients were unable to tolerate sulfathiazole and were considered to have been inadequately treated. One complete failure was noted. Organisms which were killed by sulfathiazole in this series of cases were Staphylococcus albus, Staph. aureus, Proteus vulgaris, coli, A. aerogenes, Corynebacterium xerosis and Streptococcus mitis alpha. The most resistant organism was Str. faecalis gamma. Sulfathiazole was administered to 6 additional patients only while they had acute pyelitis. Symptomatic improvement followed quickly in each case. No attempts were made to sterilize the urine of these patients, because all patients had indwelling catheters. Of the entire group of 30 patients who received sulfathiazole, toxic manifestations were experienced by 23.3 per cent. No serious end results were noted. All toxic symptoms disappeared on withdrawal of the drug. Most patients received 1 Gm. of sulfathiazole every six hours for five to ten days. The content of the drug in the blood was highest in those patients who experienced toxic symptoms, but it was less than 1 mg. per hundred cubic centimeters in the blood of several patients who were cured. The content of the drug in the urine is a more accurate index of the progress of treatment, Culp [65] stated, than is the content of the drug in the blood.

Sulfathiazole appears to be an excellent urinary antiseptic agent if it is administered under favorable conditions and with great care. The toxic symptoms which it causes makes it imperative for the physician to follow all patients at frequent intervals. Routine hospitalization should be employed if possible. Restriction of the intake of fluid should be avoided if possible.

Urologic Complications of the Use of Sulfanilamide Compounds.—Carroll, Shea and Pike [66] stated that supersaturation of acetylsulfapyridine crystals during the administration of sulfapyridine is sufficient at times to cause complete obstruction in the urinary tract. This condition can be relieved promptly and satisfactorily by the cystoscopic insertion of catheters in the ureters and pelves and by lavage with warm physiologic solution of sodium chloride or sterile water. These crystals, which cause obstruction, are not opaque to roentgen rays even in large amounts;

65. Culp, O. S.: Sulfathiazole Treatment of Urinary Tract Infections, J. Urol. **44**:116-124 (July) 1940.

66. Carroll, G.; Shea, J., and Pike, G.: Complete Anuria Due to Crystalline Concretions Following the Use of Sulfapyridine in Pneumonia, J. A. M. A. **114**: 411-412 (Feb. 3) 1940.

therefore a flat roentgenogram is of no value. Symptoms of renal colic and/or hematuria should make the physician suspicious of crystalline concretions in the urinary tract and should not be mistaken for symptoms of gastric disturbance. Hematuria noted clinically probably is the result of minute traumatization of the mucous membranes by the crystals rather than the result of damage to the renal parenchyma and therefore is of no grave consequence. The forcing of fluids in conjunction with sulfapyridine therapy probably is appropriate, since it will relieve, to some extent, supersaturation of the urine. It was incidentally suggested that supersaturation of any form of crystals in the urine may result in calculous formation. Death of Carroll, Shea and Pike's [66] patient was prevented apparently by cystoscopic manipulation, and the fact that the patient's life was saved warranted this prompt report.

Antopol [67] stated that hematuria which was only microscopically detectable was encountered in 16 of 40 cases in which patients were treated with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine). In 1 case in which necropsy was performed, calculi were not demonstrable in the urinary tract, although hemorrhagic papillitis and pyelitis had been present. Typical ureteral colic, accompanied with hematuria which disappeared promptly after discontinuance of administration of sulfapyridine, was observed. In 1 case anuria occurred two days after sulfapyridine therapy had been instituted. Residual symptoms were not present in any of the cases at the time of discharge of the patients from the hospital.

Plummer and McLellan [68] reported on 2 patients in whom renal calculi developed after sulfapyridine treatment. Existence of calculi was proved in 1 case at postmortem examination and in the other by pyelographic study. The patients in both had hematuria, and 1 also had renal colic. One had received only 11 Gm. of the drug and the other 555 Gm. Pyelograms in 1 of the 2 cases demonstrated calculi which were nonopaque to roentgen rays. The serial study indicated that later the calculi had dissolved or had been washed out and renal function had returned to normal. The features of these 2 cases, together with the experimental studies reported by other investigators, indicate that hematuria and other urinary symptoms occurring after the administration of sulfapyridine are caused by the deposition of sulfapyridine crystals and concretions in the kidneys and ureters. Frequent examination of the urine, particularly for erythrocytes, should be made during therapy with sulfapyridine. Administration of the drug should not

67. Antopol, W.: The Occurrence of Urologic Complications in Humans Following Sulfapyridine Therapy, J. Urol. **43**:589-597 (April) 1940.

68. Plummer, N., and McLellan, F.: The Production of Sulfapyridine Renal Calculi in Man Following Administration of Sulfapyridine, J. A. M. A. **114**:943-946 (March 16) 1940.

be initiated or should be done very cautiously if hematuria occurs or if the patient is known to have diminished renal function.

Stryker [69] discussed the nature of the renal lesion which sometimes occurs when therapy with sulfapyridine is employed. He reported a case in which a child 5 years old died of persistent pneumococcic meningitis. At necrosy the kidneys were greatly enlarged, weighing 85 Gm. each, as compared with a normal average weight of 25 Gm. for a patient of that age. The cut edges bulged markedly. In the calices and pelves of both kidneys was a small amount of yellow-white gravel; from the pelvis of the right kidney four calculi measuring as much as 1.5 mm. in diameter were isolated. Neither the pelvis nor the ureter was dilated. In both ureters and in the bladder there was gravel similar to that found in the kidneys; this gravel was most prominent at the entrace of the ureters into the bladder. The mucosa of the urinary tract appeared to be normal. Precipitation of acetylsulfapyridine in the kidney was observed. Stryker [69] stated that marked dilatation of the cortical tubules and glomerular spaces characteristic of the kidneys in instances of toxicity caused by sulfapyridine seems to depend on intratubular precipitation of the drug or its compounds.

URINARY SECRETION IN THE CHICKEN

Hester, Essex and Mann [70] discussed the results obtained by previous investigators and pointed out that either the figures on renal urinary output are much too high or there must be a selective resorption of water by the cloacal mucosa. They used three methods of study. First, they found that ureteral cannulization performed with local anesthesia demonstrated diuresis immediately after the operation. Figures comparable to those obtained by previous workers were obtained. Subsequently, much lower figures (2.5 cc. per half hour; 120 cc. per day) were obtained. Caffeine and dextrose were employed as diuretic agents. Solution of posterior pituitary decreased the urinary flow in 1 experiment. Second, collection of the urine was done by obstruction of the rectum when necessary and by the placing of a small funnel in the urodeum. High outputs of urine were obtained by this method as well as when the birds were disturbed. Outputs of urine were much lower when determinations were made repeatedly and when the birds were undisturbed. The third method as described by Hester, Essex and Mann [70] for collection of avian urine from exteriorized ureteral orifices is a new one. By this method much smaller amounts were obtained consistently than was possible by the other methods. The amounts

69. Stryker, W. A.: The Nature of the Renal Lesion with Sulfapyridine Therapy, J. A. M. A. **114**:953-954 (March 16) 1940.

70. Hester, H. R.; Essex, H. E., and Mann, F. C.: Secretion of Urine in the Chicken (Gallus Domesticus), Am. J. Physiol. **128**:592-602 (Feb.) 1940.

varied from 61 to 123.5 cc. in eighteen collections. The urine was thick, tenacious and mucoid and contained an abundance of urates. The oral intake of water of the birds studied was from 50 to 250 cc. daily.

The observations of Hester, Essex and Mann [70] support the belief that elimination of urine in birds is fundamentally the same as the process in mammals and that the cloaca has the same function (as a receptable) as has the urinary bladder in mammals. Diuresis can be produced by relatively minor disturbances of the bird.

UROGRAPHY

Braasch and Doss [71] stated that the difficulty of determination of the cause of stasis as visualized in the delayed urogram often diminishes the clinical value of such a urogram. It is possible that more precise methods of determining ureteropelvic physiologic conditions may aid in this respect. However, the delayed urogram often is of definite value in determination of ureteropelvic obstruction, particularly in cases in which the condition is said to be "borderline." Unless the existence of stasis can be visualized in such cases, surgical intervention usually is not indicated. The delayed urogram also may be of value in identification of doubtful roentgen shadows in the ureter or kidneys.

71. Braasch, W. F., and Doss, A. K.: The Clinical Value of the Delayed Urogram, J. Urol. **43**:617-622 (April) 1940.